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NEWS 7	APR 07	50,000 World Traditional Medicine (WTM) Patents Now Available in CAplus
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NEWS 10	JUN 18	DWPI: New coverage - French Granted Patents
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NEWS 14	JUN 21	Access an additional 1.8 million records exclusively enhanced with 1.9 million CAS Registry Numbers -- EMBASE Classic on STN
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NEWS 17	JUL 19	Enhancement of citation information in INPADOC databases provides new, more efficient competitor analyses
NEWS 18	JUL 26	CAS coverage of global patent authorities has expanded to 61 with the addition of Costa Rica
NEWS 19	SEP 15	MEDLINE Cited References provide additional revelant records with no additional searching.
NEWS 20	OCT 04	Removal of Pre-IPC 8 data fields streamlines displays in USPATFULL, USPAT2, and USPATOLD.
NEWS 21	OCT 04	Precision of EMBASE searching enhanced with new chemical name field
NEWS 22	OCT 06	Increase your retrieval consistency with new formats or for Taiwanese application numbers in CA/CAplus.
NEWS 23	OCT 21	CA/CAplus kind code changes for Chinese patents increase consistency, save time
NEWS 24	OCT 22	New version of STN Viewer preserves custom highlighting of terms when patent documents are saved in .rtf format
NEWS 25	OCT 28	INPADOCDB/INPAFAMDB: Enhancements to the US national patent classification.
NEWS 26	NOV 03	New format for Korean patent application numbers in CA/CAplus increases consistency, saves time.
NEWS 27	NOV 04	Selected STN databases scheduled for removal on December 31, 2010

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L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR

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=> s l1
SAMPLE SEARCH INITIATED 12:48:09 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      384 TO ITERATE

100.0% PROCESSED      384 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         6505 TO     8855
PROJECTED ANSWERS:               0 TO        0
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L2            0 SEA SSS SAM L1

=> s l1 full
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SEARCH TIME: 00.00.01

L3           20 SEA SSS FUL L1

=> file caplus
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                                                      ENTRY    SESSION
FULL ESTIMATED COST                                  193.01     193.45

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FILE COVERS 1907 - 10 Nov 2010  VOL 153 ISS 20
FILE LAST UPDATED: 9 Nov 2010  (20101109/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Aug 2010
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Aug 2010

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=> s l3
L4           40 L3

=> d bib abs hitstr 1-40 l4

L4   ANSWER 1 OF 40  CAPLUS  COPYRIGHT 2010 ACS on STN
AN   2009:740234  CAPLUS
DN   151:70285
TI   Compositions and methods coactivating both A1 and A2A adenosine receptors
     for the treatment and prevention of cardiovascular diseases
IN   Feldman, Arthur; Chan, Tung
PA   Thomas Jefferson University, USA
SO   PCT Int. Appl., 127pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
PI   WO 2009076580        A2    20090618    WO 2008-US86528        20081212
     WO 2009076580        A3    20090820
         W:  AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,
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             FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE,
             KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,
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ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH,
PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,
IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

	US 20100272711	A1	20101028	US 2010-747147	20100706
PRAI	US 2007-13057P	P	20071212		
	WO 2008-US86528	W	20081212		

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

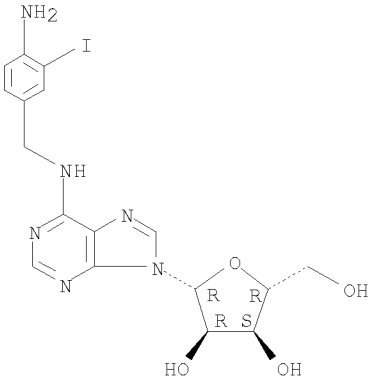
AB The present invention is directed to a pharmaceutical composition, and methods of use thereof, comprising at least one agent which target multiple adenosine receptors (AR) simultaneously in a stoichiometric relationship (i.e. each AR receptor is targeted to an equal extent). Aspects of the present invention relate to pharmaceutical compns., and uses thereof, comprising at least one agent which co-activates an A1-adenosine receptor (A1-AR) and an A2A-adenosine receptor (A2A-AR) or a combination of at least one agent which activates an A1-AR and at least one agent which activates an A2A-AR, where both the A1-AR and A2A-AR are activated in a stoichiometric relationship such that the level of biol. activation of A1-AR is approx. the same level of biol. activation of A2A-AR. Other aspects of the present invention relate to methods for the therapeutic and prophylactic treatment of cardiac dysfunction in a subject having or at risk of having a cardiac dysfunction, for example, but not limited to, for the treatment of a subject with myocardial infarction, such as acute myocardial infarction, coronary ischemia or congestive heart failure and other cardiac dysfunctions. Long term or chronic administration of agonists which activate only the A1-AR or alternatively only the A2A-AR results in deleterious effects on cardiac function. If both the A1-AR and the A2A-AR are co-activated substantially simultaneously, the cardiac function was unexpectedly not compromised. Thus, use of at least one agent which co-activates both the A1-AR and the A2A-AR, or a combination of at least one or more agents which activates the A1-AR and at least one or more agents which activate the A2A-AR is useful to mediate cardioprotective effect.

IT 98866-49-0
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(or analogs or derivs. or salts thereof, as agent activating adenosine receptor A1; compns. and methods coactivating both A1 and A2A adenosine receptors for treatment and prevention of cardiovascular diseases)

RN 98866-49-0 CAPLUS

CN Adenosine, N-[(4-amino-3-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



OSC.G 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 2 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN

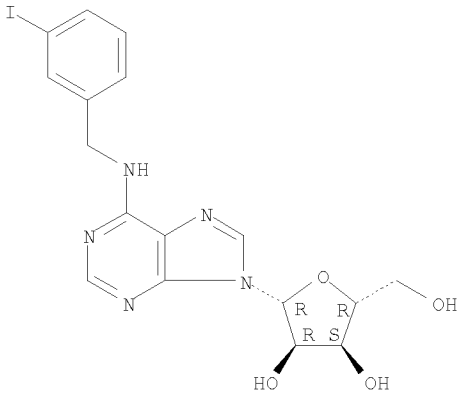
AN 2009:187579 CAPLUS

DN 150:252077

TI Flexible modulation of agonist efficacy at the human A3 adenosine receptor

by the imidazoquinoline allosteric enhancer LUF6000
AU Gao, Zhan-Guo; Ye, Kai; Goblyos, Aniko; Ijzerman, Adriaan P.; Jacobson, Kenneth A.
CS Molecular Recognition Section, Laboratory of Bioorganic Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892-0810, USA
SO BMC Pharmacology (2008), 8, No pp. given
CODEN: BPMHBU; ISSN: 1471-2210
URL: http://www.biomedcentral.com/content/pdf/1471-2210-8-20.pdf
PB BioMed Central Ltd.
DT Journal; (online computer file)
LA English
AB Background: A series of 1H-imidazo- [4,5-c]quinolin-4-amine derivs., represented by LUF6000 (N-(3,4-dichloro-phenyl)-2-cyclohexyl-1H-imidazo [4,5-c]quinolin-4-amine), are allosteric modulators of the human A3 adenosine receptor (AR). Here we studied the modulation by LUF6000 of the maximum effect (Emax) of structurally diverse agonists at the A3 AR stably expressed in CHO cells. Results: In an assay of [35S]GTPγS binding, the Emax of the A3 AR agonist Cl-IB-MECA at the A3 AR was lower than that of the non-selective AR agonist NECA. LUF6000 exerted an Emax-enhancing effect at a concentration of 0.1 μM or higher, and was shown to increase the Emax of Cl-IB-MECA and other low-efficacy agonists to a larger extent than that of the high-efficacy agonist NECA. Interestingly, LUF6000 converted a nucleoside A3 AR antagonist MRS542, but not a non-nucleoside antagonist MRS1220, into an agonist. LUF6000 alone did not show any effect. Math. modeling was performed to explain the differential effects of LUF6000 on agonists with various Emax. A simple explanation for the observation that LUF6000 has a much stronger effect on Cl-IB-MECA than on NECA derived from the math. modeling is that NECA has relatively strong intrinsic efficacy, such that the response is already close to the maximum response. Therefore, LUF6000 cannot enhance Emax much further. Conclusion: LUF6000 was found to be an allosteric enhancer of Emax of structurally diverse agonists at the A3 AR, being more effective for low-Emax agonists than for high-Emax agonists. LUF6000 was demonstrated to convert an antagonist into an agonist, which represents the first example in G protein-coupled receptors. The observations from the present study are consistent with that predicted by math. modeling.
IT 163152-30-5, MRS541
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(flexible modulation of agonist efficacy at human A3 adenosine receptor by imidazoquinoline allosteric enhancer LUF6000)
RN 163152-30-5 CAPLUS
CN Adenosine, N-[(3-iodophenyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.

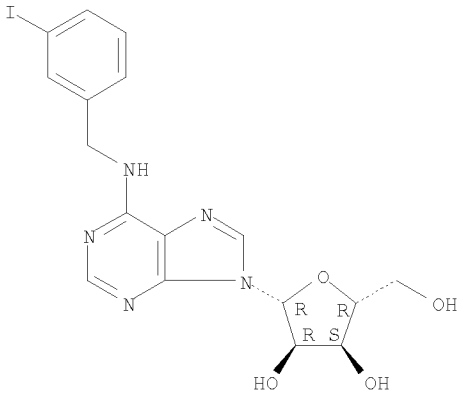


OSC.G 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2007:596054 CAPLUS
DN 147:206160

TI Probing the Binding Site of the A1 Adenosine Receptor Reengineered for Orthogonal Recognition by Tailored Nucleosides
AU Palaniappan, Krishnan K.; Gao, Zhan-Guo; Ivanov, Andrei A.; Greaves, Rebecca; Adachi, Hayamitsu; Besada, Pedro; Kim, Hea Ok; Kim, Ae Yil; Choe, Seung Ah; Jeong, Lak Shin; Jacobson, Kenneth A.
CS Molecular Recognition Section, Laboratory of Bioorganic Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892, USA
SO Biochemistry (2007), 46(25), 7437-7448
CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
OS CASREACT 147:206160
AB His272 (7.43) in the seventh transmembrane domain (TM7) of the human A3 adenosine receptor (AR) interacts with the 3' position of nucleosides, based on selective affinity enhancement at a H272E mutant A3 AR (neoceptor) of 3'-ureido, but not 3'-OH, adenosine analogs. Here, mutation of the analogous H278 of the human A1 AR to Ala, Asp, Glu, or Leu enhanced the affinity of novel 2'- and 3'-ureido adenosine analogs, such as 10 (N6-cyclopentyl-3'-ureido-3'-deoxyadenosine), by >100-fold, while decreasing the affinity or potency of adenosine and other 3'-OH adenosine analogs. His278 mutant receptors produced a similar enhancement regardless of the charge character of the substituted residue, implicating steric rather than electrostatic factors in the gain of function, a hypothesis supported by rhodopsin-based mol. modeling. It was also demonstrated that this interaction was orientationally specific; i.e., mutations at the neighboring Thr277 did not enhance the affinity for a series of 2'- and 3'-ureido nucleosides. Addnl., H-bonding groups placed on substituents at the N6 or 5' position demonstrated no enhancement in the mutant receptors. These reengineered human A1 ARs revealed orthogonality similar to that of the A3 but not the A2A AR, in which mutation of the corresponding residue, His278, to Asp did not enhance nucleoside affinity. Functionally, the H278D A1 AR was detectable only in a measure of membrane potential and not in calcium mobilization. This neoceptor approach should be useful for the validation of mol. modeling and the dissection of promiscuous GPCR signaling.
IT 163152-30-5
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(probing binding site of A1 adenosine receptor reengineered for orthogonal recognition by tailored nucleosides)
RN 163152-30-5 CAPLUS
CN Adenosine, N-[(3-iodophenyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



OSC.G 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2007:474159 CAPLUS
DN 147:143613

TI Preparation, biological activity and endogenous occurrence of N6-benzyladenosines

AU Dolezal, Karel; Popa, Igor; Hauserova, Eva; Spichal, Lukas; Chakrabarty, Kuheli; Novak, Ondrej; Krystof, Vladimir; Voller, Jiri; Holub, Jan; Strnad, Miroslav

CS Laboratory of Growth Regulators, Palacky University & Institute of Experimental Botany AS CR, Olomouc, 783 71, Czech Rep.

SO Bioorganic & Medicinal Chemistry (2007), 15(11), 3737-3747
CODEN: BMECEP; ISSN: 0968-0896

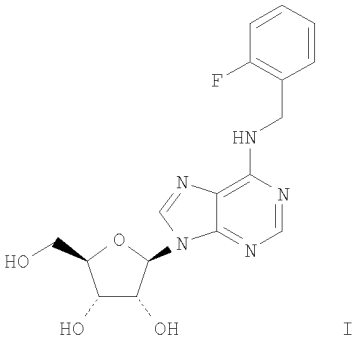
PB Elsevier Ltd.

DT Journal

LA English

OS CASREACT 147:143613

GI



I

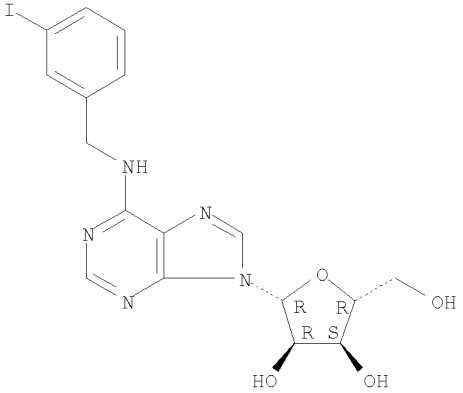
AB Cytokinin activity of forty-eight 6-benzyladenosine derivs., e.g. I, at both the receptor and cellular levels as well as their anticancer properties were compared in various in vitro assays. The compds. were prepared by the condensation of 6-chloropurine riboside with corresponding substituted benzylamines and characterized by standard collection of physico-chemical methods. The majority of synthesized derivs. exhibited high activity in all three of the cytokinin bioassays used (tobacco callus, wheat leaf senescence and Amaranthus bioassay). The highest activities were observed in the senescence bioassay. For several of the compds. tested, significant differences in activity were found between the bioassays used, indicating that diverse recognition systems may operate. This suggests that it may be possible to modulate particular cytokinin-dependent processes with specific compds. In contrast to their high activity in bioassays, the tested compds. were recognized with only very low sensitivity in both Arabidopsis thaliana AHK3 and AHK4 receptor assays. The prepared derivs. were also investigated for their antiproliferative properties on cancer and normal cell lines. Several of them showed very strong cytotoxic activity against various cancer cell lines. On the other hand, they were not cytotoxic for normal murine fibroblast (NIH/3T3) cell line. This anticancer activity of cytokinin ribosides may be important, given that several of them occur as endogenous compds. in different organisms.

IT 163152-30-5P
RL: AGR (Agricultural use); PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzyladenosines via condensation of chloropurine riboside with benzylamines, and their cytokinin, antitumor activity and endogenous occurrence)

RN 163152-30-5 CAPLUS

CN Adenosine, N-[(3-iodophenyl)methyl]- (CA INDEX NAME)

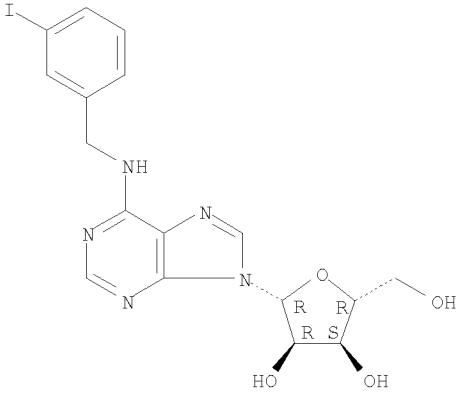
Absolute stereochemistry.



OSC.G 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2007:245615 CAPLUS
DN 146:474750
TI Three-Dimensional Quantitative Structure-Activity Relationship of Nucleosides Acting at the A3 Adenosine Receptor: Analysis of Binding and Relative Efficacy
AU Kim, Soo-Kyung; Jacobson, Kenneth A.
CS Molecular Recognition Section Laboratory of Bioorganic Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH), Bethesda, MD, 20892, USA
SO Journal of Chemical Information and Modeling (2007), 47(3), 1225-1233
CODEN: JCISD8; ISSN: 1549-9596
PB American Chemical Society
DT Journal
LA English
AB The binding affinity and relative maximal efficacy of human A3 adenosine receptor (AR) agonists were each subjected to ligand-based three-dimensional quant. structure-activity relation anal. Comparative mol. field anal. (CoMFA) and comparative mol. similarity indexes anal. (CoMSIA) used as training sets a series of 91 structurally diverse adenosine analogs with modifications at the N6 and C2 positions of the adenine ring and at the 3', 4', and 5' positions of the ribose moiety. The CoMFA and CoMSIA models yielded significant cross-validated q2 values of 0.53 (r2 = 0.92) and 0.59 (r2 = 0.92), resp., and were further validated by an external test set (25 adenosine derivs.), resulting in the best predictive r2 values of 0.84 and 0.70 in each model. Both the CoMFA and the CoMSIA maps for steric or hydrophobic, electrostatic, and hydrogen-bonding interactions well reflected the nature of the putative binding site previously obtained by mol. docking. A conformationally restricted bulky group at the N6 or C2 position of the adenine ring and a hydrophilic and/or H-bonding group at the 5' position were predicted to increase A3AR binding affinity. A small hydrophobic group at N6 promotes receptor activation. A hydrophilic and hydrogen-bonding moiety at the 5' position appears to contribute to the receptor activation process, associated with the conformational change of transmembrane domains 5, 6, and 7. The 3D-CoMFA/CoMSIA model correlates well with previous receptor-docking results, current data of A3AR agonists, and the successful conversion of the A3AR agonist into antagonists by substitution (at N6) or conformational constraint (at 5'-N-methyluronamide).
IT 163152-30-5
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(QSAR of nucleosides acting at A3 adenosine receptor)
RN 163152-30-5 CAPLUS
CN Adenosine, N-[(3-iodophenyl)methyl]- (CA INDEX NAME)

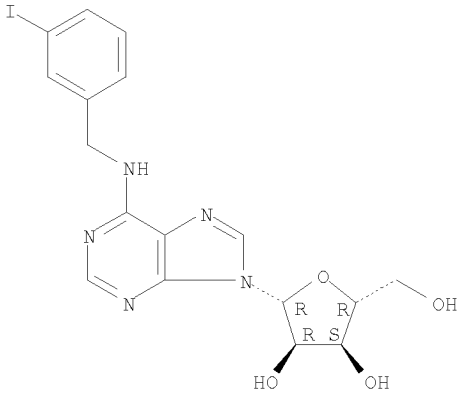
Absolute stereochemistry.



OSC.G 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2006:1172157 CAPLUS
DN 146:93671
TI Docking studies of agonists and antagonists suggest an activation pathway of the A3 adenosine receptor
AU Kim, Soo-Kyung; Gao, Zhan-Guo; Jeong, Lak Shin; Jacobson, Kenneth A.
CS Molecular Recognition Section, Laboratory of Bioorganic Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH), Bethesda, MD, 20892, USA
SO Journal of Molecular Graphics & Modelling (2006), 25(4), 562-577
CODEN: JMGMFI; ISSN: 1093-3263
PB Elsevier Inc.
DT Journal
LA English
AB Structural determinants of ligand efficacy in the human A3 adenosine receptor (AR) were studied using pharmacophore and docking analyses of various categories of A3 selective ligands: inverse agonist, neutral antagonist (nonnucleoside and nucleoside), and agonist (partial and full). The homol. modeling of GPCRs was adapted to provide two templates: the rhodopsin-based resting state for antagonist binding and a putative Meta I state, conformationally altered at a key residue (W6.48), for agonist binding. The preferential binding domains and/or local conformational changes associated with docking of three high affinity A3AR ligands were compared: inverse agonist PSB-11, neutral antagonist MRE-3008F20, and full agonist Cl-IB-MECA to define a distinct recognition mode for each. Ribose-containing agonists were more hydrophilic than nonnucleoside antagonists, and H-bonding ability at the ribose 3'- and 5'-positions was required for agonism. From the receptor perspective, common requirements for activation included the destabilization of H-bond networks at W6.48 and H7.43, the specific interactions of the ribose moiety in its putative hydrophilic pocket at T3.36, S7.42, and H7.43, the stabilization of the complex by inward movement of F5.43, and the characteristic rotation of W6.48. By analogy, outward rotation of the W6.48 side-chain upon activation of an internally-crosslinking mutant M3 muscarinic receptor was indicated by constrained mol. dynamics (MD). The authors' results are consistent with an anti-clockwise rotation (from the extracellular view) of transmembrane domains 3, 5, 6, and 7, as proposed for other Family A GPCRs. Thus, the putative conformational changes associated with A3AR activation indicate a shared mechanism of GPCR activation similar to rhodopsin.
IT 163152-30-5, MRS 541
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(combination of docking studies and pharmacophore anal. of mol. mechanisms of interaction of agonists and antagonists with human adenosine A3 receptors)
RN 163152-30-5 CAPLUS
CN Adenosine, N-[(3-iodophenyl)methyl]- (CA INDEX NAME)

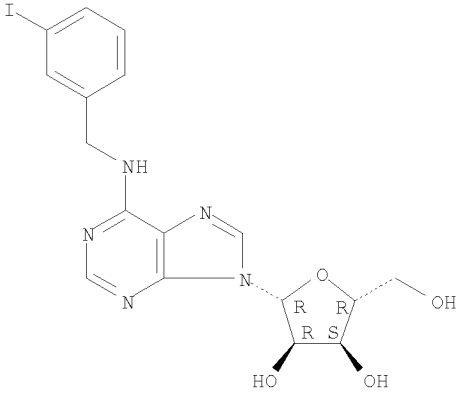
Absolute stereochemistry.



OSC.G 26 THERE ARE 26 CAPLUS RECORDS THAT CITE THIS RECORD (26 CITINGS)
RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2005:1341969 CAPLUS
DN 144:233314
TI Conversion of A3 adenosine receptor agonists into selective antagonists by modification of the 5'-ribofuran-uronamide moiety
AU Gao, Zhan-Guo; Joshi, Bhalchandra V.; Klutz, Athena M.; Kim, Soo-Kyung; Lee, Hyuk Woo; Kim, Hea Ok; Jeong, Lak Shin; Jacobson, Kenneth A.
CS Molecular Recognition Section, Laboratory of Bioorganic Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892, USA
SO Bioorganic & Medicinal Chemistry Letters (2006), 16(3), 596-601
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 144:233314
AB The highly selective agonists of the A3 adenosine receptor (AR), Cl-IB-MECA (2-chloro-N6-(3-iodobenzyl)-5'-N-methylcarboxamidoadenosine), and its 4'-thio analog, were successfully converted into selective antagonists simply by appending a second N-Me group on the 5'-uronamide position. The 2-chloro-5'-(N,N-dimethyl)uronamido analogs bound to, but did not activate, the human A3AR, with Ki values of 29 nM (4'-O) and 15 nM (4'-S), showing >100-fold selectivity over A1, A2A, and A2BARs. Competitive antagonism was demonstrated by Schild anal. The 2-(dimethylamino)-5'-(N,N-dimethyl)uronamido substitution also retained A3AR selectivity but lowered affinity.
IT 163152-30-5
RL: PAC (Pharmacological activity); BIOL (Biological study)
(conversion of A3 adenosine receptor agonists into selective antagonists by modification of the 5'-ribofuran-uronamide moiety)
RN 163152-30-5 CAPLUS
CN Adenosine, N-[(3-iodophenyl)methyl]- (CA INDEX NAME)

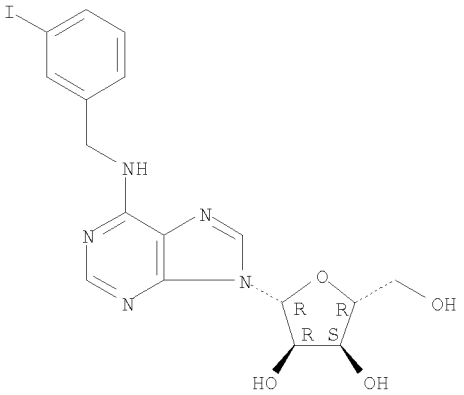
Absolute stereochemistry.



OSC.G 24 THERE ARE 24 CAPLUS RECORDS THAT CITE THIS RECORD (24 CITINGS)
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2005:100499 CAPLUS
DN 142:355510
TI Synthesis, Biological Evaluation, and Molecular Modeling of Ribose-Modified Adenosine Analogues as Adenosine Receptor Agonists
AU Cappellacci, Loredana; Franchetti, Palmarisa; Pasqualini, Michela; Petrelli, Riccardo; Vita, Patrizia; Lavecchia, Antonio; Novellino, Ettore; Costa, Barbara; Martini, Claudia; Klotz, Karl-Norbert; Grifantini, Mario
CS Dipartimento di Scienze Chimiche, Universita di Camerino, Camerino, 62032, Italy
SO Journal of Medicinal Chemistry (2005), 48(5), 1550-1562
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 142:355510
AB A number of 3'-C-Me analogs of selective adenosine receptor agonists such as CPA, CHA, CCPA, 2'-Me-CCPA, NECA, and IB-MECA was synthesized to further investigate the sub-domain of the receptor that binds the ribose moiety of the ligands. Affinity data at A1, A2A, and A3 receptors in bovine brain membranes showed that the 3'-C-modification in adenosine resulted in a decrease of the affinity at all three receptor subtypes. When this modification was combined with N6-substitution with groups that induce high potency and selectivity at A1 receptor, the affinity and selectivity were increased. However, all 3'-C-Me derivs. proved to be very less active than the corresponding 2'-C-Me analogs. The most active compound was found to be 3'-Me-CPA which displayed a Ki value of 0.35 μM at A1 receptor and a selectivity for A1 vs A2A and A3 receptors higher than 28-fold. 2'-Me-CCPA was confirmed to be the most selective, high affinity agonist so far known also at human A1 receptor with a Ki value of 3.3 nM and 2903- and 341-fold selective vs human A2A and A3 receptors, resp. In functional assay, 3'-Me-CPA, 3'-Me-CCPA, and 2-Cl-3'-Me-IB-MECA inhibited forskolin-stimulated adenylyl cyclase activity with IC50 values ranging from 0.3 to 4.9 μM, acting as full agonists. A rhodopsin-based model of the bovine A1AR was built to rationalize the higher affinity and selectivity of 2'-C-Me derivs. of N6-substituted-adenosine compared to that of 3'-C-Me analogs. In the docking exploration, it was found that 2'-Me-CCPA was able to form a number of interactions with several polar residues in the transmembrane helixes TM-3, TM-6, and TM-7 of bA1AR which were not preserved in the mol. dynamics simulation of 3'-Me-CCPA/bA1AR complex.
IT 163152-30-5
RL: PAC (Pharmacological activity); BIOL (Biological study)
(synthesis biol. evaluation and mol. modeling of ribose-modified adenosine analogs as adenosine receptor agonists)
RN 163152-30-5 CAPLUS
CN Adenosine, N-[(3-iodophenyl)methyl]- (CA INDEX NAME)

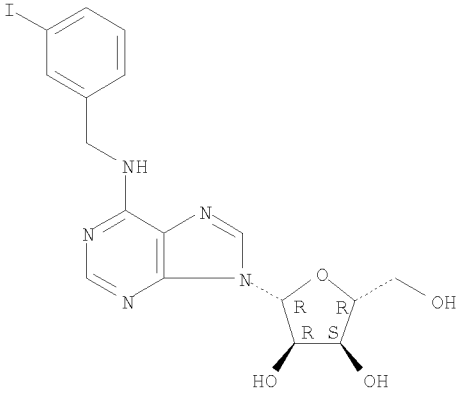
Absolute stereochemistry.



OSC.G 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (21 CITINGS)
RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2005:44237 CAPLUS
DN 142:290603
TI A radial distribution function approach to predict A2B agonist effect of adenosine analogues
AU Gonzalez, Maykel Perez; Teran, Carmen; Fall, Yagamare; Teijeira, Marta; Besada, Pedro
CS Unit of Services, Department of Drug Design, Experimental Sugar Cane Station 'Villa Clara-Cienfuegos', Ranchuelo, Cuba
SO Bioorganic & Medicinal Chemistry (2005), 13(3), 601-608
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Ltd.
DT Journal
LA English
AB The radial distribution function (RDF) approach has been applied to the study of the A2B agonist effect of a set of 89 adenosine analogs reported with this activity. A model able to describe more than 70% of the variance in the exptl. activity was developed with the use of the mentioned approach. In contrast, none of the eleven different approaches including the use of Constitutional, Topol., Mol. walk count, BCUT, Galvez topol. charge indexes, 2D autocorrelations, Randic mol. profiles, Geometrical, 3D Morse, WHIM and GETAWAY descriptors was able to explain more than 47% of the variance in the mentioned property with the same number of descriptors.
IT 163152-30-5
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(radial distribution function approach to predict A2B agonist effect of adenosine analogs)
RN 163152-30-5 CAPLUS
CN Adenosine, N-[(3-iodophenyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



OSC.G 21 THERE ARE 21 CAPLUS RECORDS THAT CITE THIS RECORD (21 CITINGS)
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2005:34766 CAPLUS
DN 142:127629
TI Compositions and methods for use of a protease inhibitor and adenosine for preventing organ ischemia and reperfusion injury
IN Vinten-Johansen, Jakob
PA Emory University, USA
SO PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005003150	A2	20050113	WO 2004-US21387	20040702
	WO 2005003150	A3	20051013		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2531062	A1	20050113	CA 2004-2531062	20040702
	EP 1638579	A2	20060329	EP 2004-756603	20040702
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
	US 20060205671	A1	20060914	US 2006-562757	20060328
PRAI	US 2003-484484P	P	20030702		
	WO 2004-US21387	W	20040702		

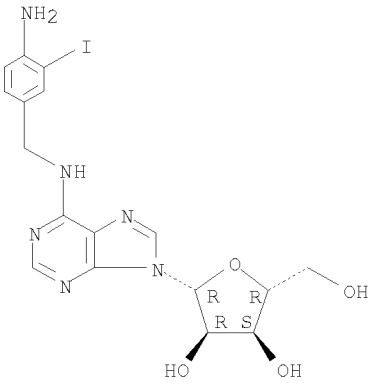
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Methods and compns. including combined use of a serine protease inhibitor and adenosine or adenosine agonist when administered as a single pharmaceutical composition, concomitantly or sequentially in any order to a living subject for preventing organ ischemia or reperfusion injury. The methods and compns. disclosed herein can be used in such procedures as cardiac surgery, non-surgical cardiac revascularization, organ transplantation, perfusion, ischemia, reperfusion, ischemia-reperfusion injury, oxidant injury, cytokine induced injury, shock induced injury, resuscitations injury or apoptosis.

IT 98866-49-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of a serine protease inhibitor and adenosine agonist for preventing organ ischemia and reperfusion injury in relation to alteration of G protein-coupled receptors and cAMP)

RN 98866-49-0 CAPLUS
CN Adenosine, N-[(4-amino-3-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

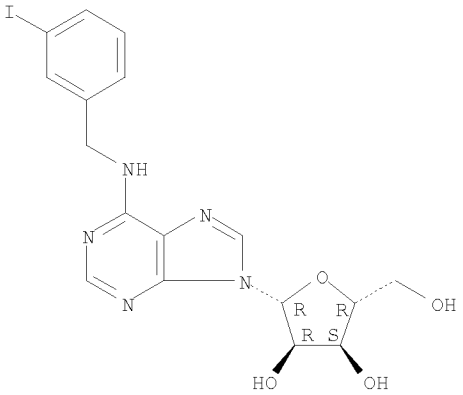
Absolute stereochemistry.



L4 ANSWER 11 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2004:773120 CAPLUS
DN 142:219479
TI (N)-Methanocarba 2,N6-Disubstituted Adenine Nucleosides as Highly Potent and Selective A3 Adenosine Receptor Agonists
AU Tchilibon, Susanna; Joshi, Bhalchandra V.; Kim, Soo-Kyung; Duong, Heng T.; Gao, Zhan-Guo; Jacobson, Kenneth A.
CS Molecular Recognition Section Laboratory of Bioorganic Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases National Institutes of Health, Bethesda, MD, 20892, USA
SO Journal of Medicinal Chemistry (2005), 48(6), 1745-1758
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 142:219479
AB A series of ring-constrained (N)-methanocarba-5'-uronamide 2,N6-disubstituted adenine nucleosides have been synthesized via Mitsunobu condensation of the nucleobase precursor with a pseudosugar ring containing a 5'-ester functionality. Following appropriate functionalization of the adenine ring, the ester group was converted to the 5'-N-methylamide. The compds., mainly 2-chloro-substituted derivs., were tested in both binding and functional assays at human adenosine receptors (ARs), and many were found to be highly potent and selective A3AR agonists. Selected compds. were compared in binding to the rat A3AR to assess their viability for testing in rat disease models. The N6-(3-chlorobenzyl) and N6-(3-bromobenzyl) analogs displayed Ki values at the human A3AR of 0.29 and 0.38 nM, resp. Other subnanomolar affinities were observed for the following N6 derivs.: 2,5-dichlorobenzyl, 5-iodo-2-methoxybenzyl, trans-2-phenyl-1-cyclopropyl, and 2,2-diphenylethyl. Selectivity for the human A3AR in comparison to the A1AR was the following (fold): the N6-(2,2-diphenylethyl) analog (1900), the N6-(2,5-dimethoxybenzyl) analog (1200), the N6-(2,5-dichlorobenzyl) and N6-(2-phenyl-1-cyclopropyl) analogs (1000), and the N6-(3-substituted benzyl) analogs (700-900). Typically, even greater selectivity ratios were obtained in comparison with the A2A and A2BARs. The (N)-methanocarba-5'-uronamide analogs were full agonists at the A3AR, as indicated by the inhibition of forskolin-stimulated adenylate cyclase at a concentration of 10 μM. The N6-(2,2-diphenylethyl) derivative was an A3AR agonist in the (N)-methanocarba-5'-uronamide series, although it was an antagonist in the ribose series. Thus, many of the previously known groups that enhance A3AR affinity in the 9-riboside series, including those that reduce intrinsic efficacy, may be adapted to the (N)-methanocarba nucleoside series of full agonists.
IT 163152-30-5
RL: PAC (Pharmacological activity); BIOL (Biological study)
(synthesis of methanocarba disubstituted adenine nucleosides as highly potent and selective A3 adenosine receptor agonists)

RN 163152-30-5 CAPLUS
CN Adenosine, N-[(3-iodophenyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



OSC.G 44 THERE ARE 44 CAPLUS RECORDS THAT CITE THIS RECORD (46 CITINGS)
RE.CNT 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2004:566634 CAPLUS
DN 141:123865
TI Substitution derivatives of N6-benzyl-adenosine, methods of their preparation, their use for preparation of drugs, cosmetic preparations and growth regulators, pharmaceutical preparations, cosmetic preparations and growth regulators containing these compounds
IN Dolezal, Karel; Popa, Igor; Zatloukal, Marek; Lenobel, Rene; Hradecka, Dana; Vojtesek, Borivoj; Uldrijan, Stjepan; Mlejnek, Petr; Werbrouck, Stefaan; Strnad, Miroslav
PA Ustav Experimentalni Botaniky Akademie Ved Ceske Republiky, Czech Rep.; et al.
SO PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

my 10/540993 application

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004058791	A2	20040715	WO 2003-CZ78	20031229
	WO 2004058791	A3	20041028		
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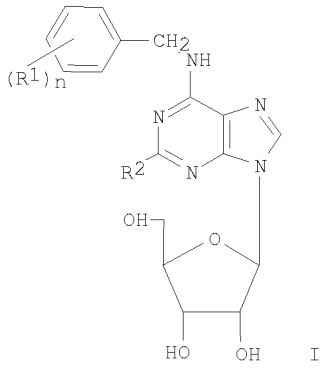
	CZ 294538	B6	20050112	CZ 2002-4273	20021230
	AU 2003294608	A1	20040722	AU 2003-294608	20031229
	EP 1575973	A2	20050921	EP 2003-785482	20031229
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	ZA 2005006074	A	20060531	ZA 2005-6074	20050728
	US 20060166925	A1	20060727	US 2005-540993	20050815
PRAI	CZ 2002-4273	A	20021230		
	WO 2003-CZ78	W	20031229		

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OS MARPAT 141:123865
GI



I

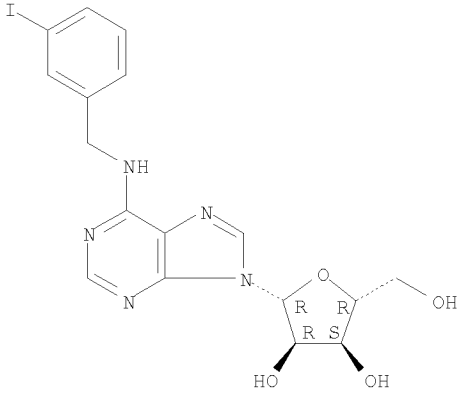
AB The invention concerns novel substitution derivs. of N6-benzyl-adenosine I, wherein n is 2-6; R1 is H, OH, halogen, alkoxy, amino, hydrazo, mercapto, methylmercapto, carboxyl, cyano, nitro, amido, sulfo, sulfamido, acylamino, acyloxy, alkylamino, dialkylamino, alkylmercapto, carbylalkoxy, cycloalkyl, carbamoyl alkyl; R2 is H, OH, halogen, alkoxy, amino, hydrazo, mercapto, methylmercapto, carboxyl, cyano, nitro, amido, sulfo, sulfamido, acylamino, acyloxy, alkylamino, dialkylamino, alkylmercapto, cabylalkoxy, cycloalkyl, carbamoyl, having anticancer, mitotic, immunosuppressive and anti-senescent properties for plant, animal and human cells. This invention also relates to the methods of preparation of these N6-benzyl-adenosine derivs. and their use as drugs, cosmetic prepns. and growth regulators comprising these derivs. as active compound and use of these derivs. for preparation of pharmaceutical compns., in biotechnol. processes, in cosmetics and in agriculture. Use of title compds. as mitotic or antimitotic compound, especially for treating cancer, psoriasis, rheumatoid arthritis, lupus, type I diabetes, multiple sclerosis, restenosis, polycystic kidney disease, graft rejection, graft vs. host disease and gout, parasitoses such as those caused by fungi or protists, or Alzheimer's disease, or as anti-neurogenerative drugs, or to suppress immunostimulation or for the treatment of proliferative skin diseases. Thus, 2-amino-6-(2-methoxybenzylamino)purine riboside was prepared as growth regulator, and antitumor agent.

IT 163152-30-5P 722505-02-4P 722505-03-5P
722505-04-6P 722505-05-7P 722505-06-8P
722505-07-9P 722505-08-0P 722505-09-1P
722505-10-4P 722505-11-5P 722505-12-6P
722505-31-9P 722506-34-5P 722506-35-6P
722506-74-3P
RL: AGR (Agricultural use); BSU (Biological study, unclassified); COS (Cosmetic use); IMF (Industrial manufacture); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N6-benzyladenosine nucleosides as antitumor, mitotic, immunosuppressive prodrugs, cosmetic agents, and growth regulators)

RN 163152-30-5 CAPLUS

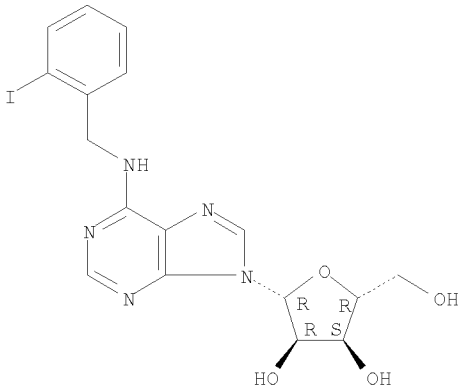
CN Adenosine, N-[(3-iodophenyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



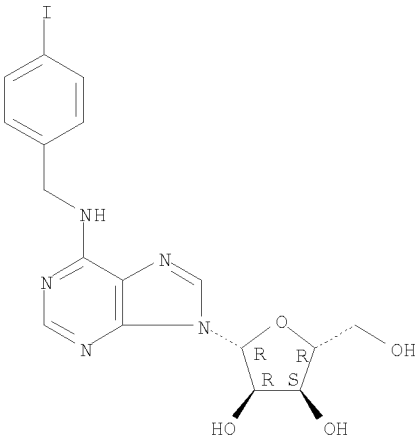
RN 722505-02-4 CAPLUS
CN Adenosine, N-[(2-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



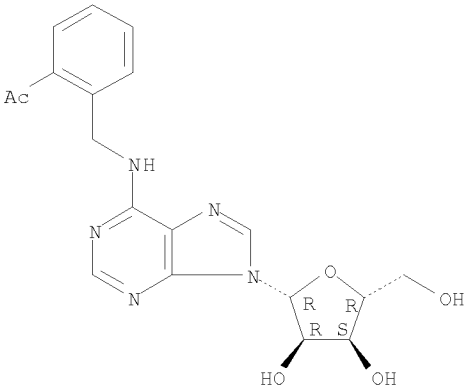
RN 722505-03-5 CAPLUS
CN Adenosine, N-[(4-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



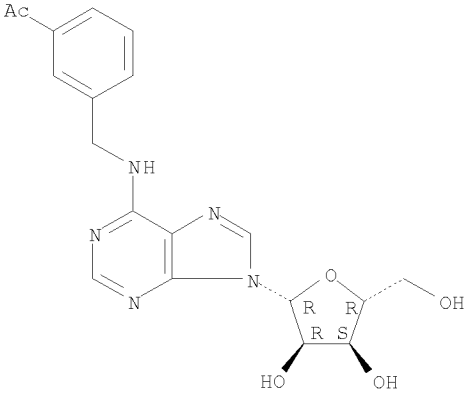
RN 722505-04-6 CAPLUS
CN Adenosine, N-[(2-acetylphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



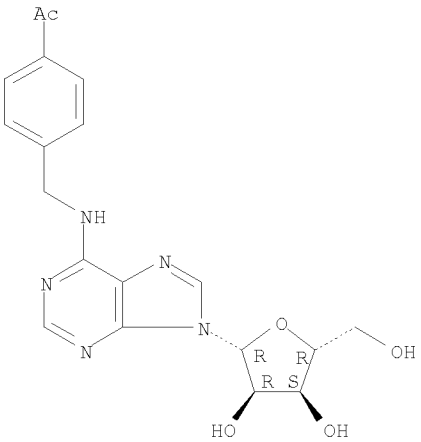
RN 722505-05-7 CAPLUS
CN Adenosine, N-[(3-acetylphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



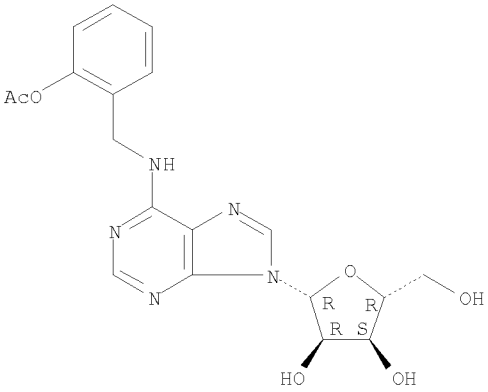
RN 722505-06-8 CAPLUS
CN Adenosine, N-[(4-acetylphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



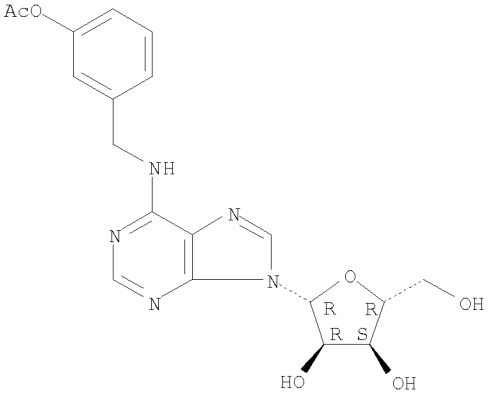
RN 722505-07-9 CAPLUS
CN Adenosine, N-[[2-(acetyloxy)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



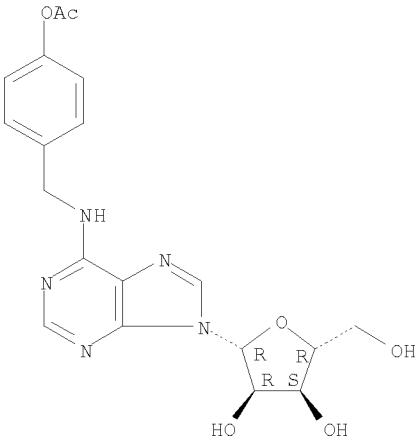
RN 722505-08-0 CAPLUS
CN Adenosine, N-[[3-(acetyloxy)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 722505-09-1 CAPLUS
CN Adenosine, N-[[4-(acetyloxy)phenyl]methyl]- (9CI) (CA INDEX NAME)

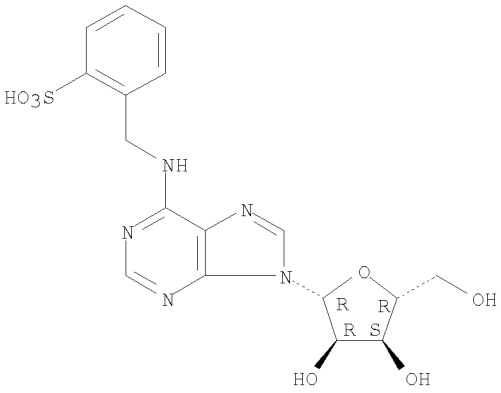
Absolute stereochemistry.



RN 722505-10-4 CAPLUS
CN Benzenesulfonic acid, 2-[[(9-β-D-ribofuranosyl-9H-purin-6-

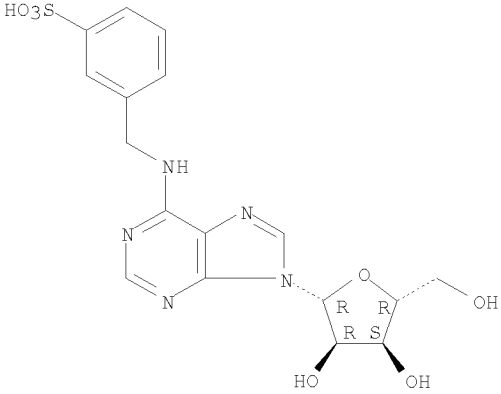
yl)amino]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



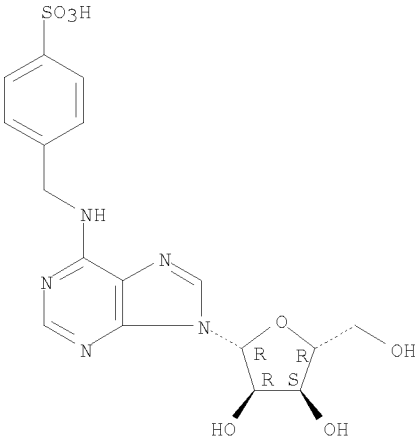
RN 722505-11-5 CAPLUS
CN Benzenesulfonic acid, 3-[[(9-β-D-ribofuranosyl-9H-purin-6-yl)amino]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



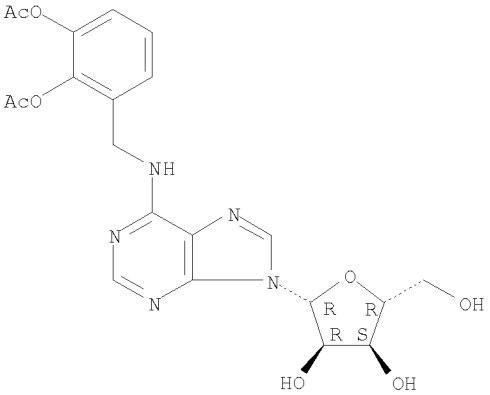
RN 722505-12-6 CAPLUS
CN Benzenesulfonic acid, 4-[[(9-β-D-ribofuranosyl-9H-purin-6-yl)amino]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



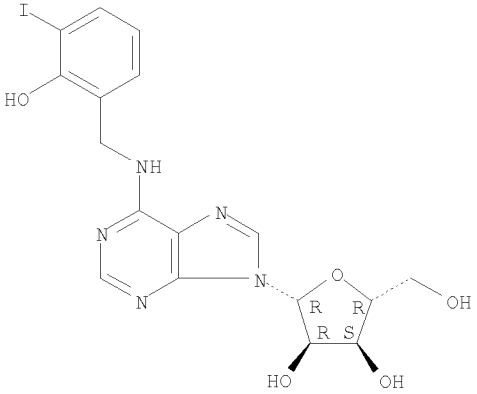
RN 722505-31-9 CAPLUS
CN Adenosine, N-[[2,3-bis(acetyloxy)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



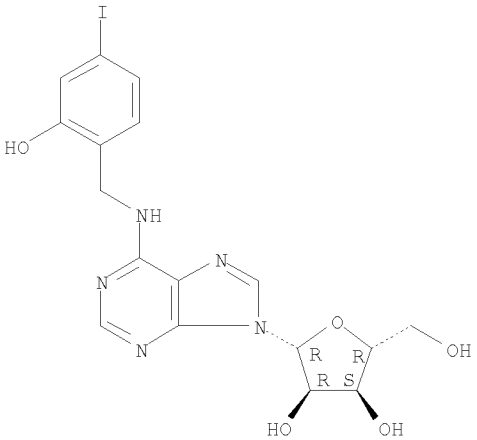
RN 722506-34-5 CAPLUS
CN Adenosine, N-[(2-hydroxy-3-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



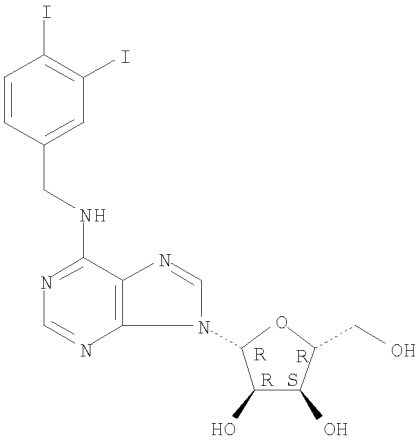
RN 722506-35-6 CAPLUS
CN Adenosine, N-[(2-hydroxy-4-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 722506-74-3 CAPLUS
CN Adenosine, N-[(3,4-diiodophenyl)methyl]- (9CI) (CA INDEX NAME)

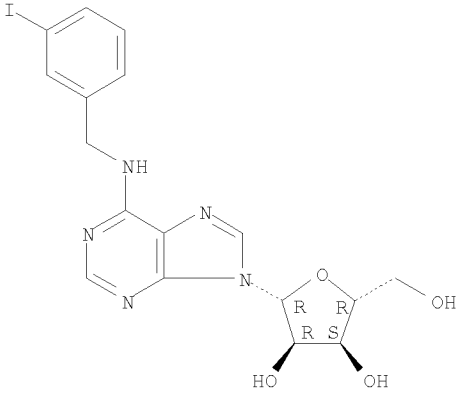
Absolute stereochemistry.



OSC.G 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2004:406956 CAPLUS
DN 141:235647
TI Modulation of adenosine receptor affinity and intrinsic efficacy in adenine nucleosides substituted at the 2-position
AU Ohno, Michihiro; Gao, Zhan-Guo; Van Rompaey, Philippe; Tchilibon, Susanna; Kim, Soo-Kyung; Harris, Brian A.; Gross, Ariel S.; Duong, Heng T.; Van Calenbergh, Serge; Jacobson, Kenneth A.
CS National Institute of Diabetes and Digestive and Kidney Diseases, DHHS, Laboratory of Bioorganic Chemistry, Molecular Recognition Section, National Institutes of Health (NIH), Bethesda, MD, 20892-0810, USA
SO Bioorganic & Medicinal Chemistry (2004), 12(11), 2995-3007
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Ltd.
DT Journal
LA English
OS CASREACT 141:235647
AB We studied the structural determinants of binding affinity and efficacy of adenosine receptor (AR) agonists. Substituents at the 2-position of adenosine were combined with N6-substitutions known to enhance human A3AR affinity. Selectivity of binding of the analogs and their functional effects on cAMP production were studied using recombinant human A1, A2A, A2B, and A3ARs. Mainly sterically small substituents at the 2-position modulated both the affinity and intrinsic efficacy at all subtypes. The 2-cyano group decreased hA3AR affinity and efficacy in the cases of N6-(3-iodobenzyl) and N6-(trans-2-phenyl-1-cyclopropyl), for which a full A3AR agonist was converted into a selective antagonist; the 2-cyano-N6-Me analog was a full A3AR agonist. The combination of N6-benzyl and various 2-substitutions (chloro, trifluoromethyl, and cyano) resulted in reduced efficacy at the A1AR. The environment surrounding the 2-position within the putative A3AR binding site was explored using rhodopsin-based homol. modeling and ligand docking.
IT 163152-30-5
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(modulation of adenosine receptor affinity and intrinsic efficacy in adenine nucleosides substituted at the 2-position)
RN 163152-30-5 CAPLUS
CN Adenosine, N-[(3-iodophenyl)methyl]- (CA INDEX NAME)

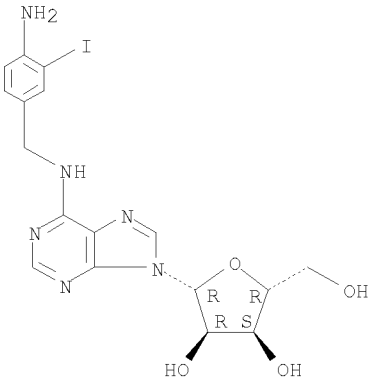
Absolute stereochemistry.



OSC.G 31 THERE ARE 31 CAPLUS RECORDS THAT CITE THIS RECORD (31 CITINGS)
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2004:406955 CAPLUS
DN 141:64408
TI A TOPS-MODE approach to predict affinity for A1 adenosine receptors. 2-(Arylamino)adenosine analogues
AU Perez Gonzalez, Maykel; Teran Moldes, Maria del Carmen
CS Experimental Sugar Cane Station "Villa Clara-Cienfuegos", Services Unit, Drug Design Department, Ranchuelo, 53100, Cuba
SO Bioorganic & Medicinal Chemistry (2004), 12(11), 2985-2993
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Ltd.
DT Journal
LA English
AB The TOPol. Sub-Structural Mol. Design (TOPS-MODE) approach has been applied to the study of the affinity of A1 adenosine receptor of different 2-(arylamino)adenosine analogs. A model able to describe closed to 79% of the variance in the values for binding expts. of 32 analogs of these compds. through multilinear regression anal. (MRA) was developed with the use of the mentioned approach. In contrast, no one of seven different approaches, including the use of Constitutional, Topol., Mol. walk counts, BCUT, Randic Mol. profiles, Geometrical, and RDF descriptors was able to explain more than 70% of the variance in the mentioned property with the same number of descriptors. In addition, the TOPS-MODE approach permitted to find the contribution of different fragments to the biol. property giving to the model a straightforward structural interpretability.
IT 98866-49-0
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(TOPS-MODE approach to predict affinity for A1 adenosine receptors, studied using 2-(arylamino)adenosine analogs)
RN 98866-49-0 CAPLUS
CN Adenosine, N-[(4-amino-3-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

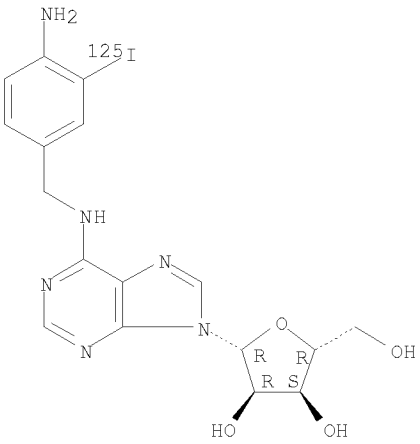
Absolute stereochemistry.



RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

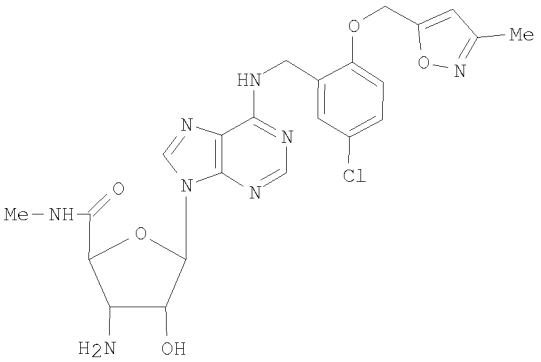
L4 ANSWER 15 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2003:967197 CAPLUS
DN 140:193623
TI Allosteric enhancers of A1 adenosine receptors increase receptor-G protein coupling and counteract guanine nucleotide effects on agonist binding
AU Figler, Heidi; Olsson, Ray A.; Linden, Joel
CS Cardiovascular Research Center, University of Virginia, Charlottesville, VA, USA
SO Molecular Pharmacology (2003), 64(6), 1557-1564
CODEN: MOPMA3; ISSN: 0026-895X
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB Endogenous ligands of G protein-coupled receptors bind to orthosteric sites that are topol. distinct from allosteric sites. Certain aminothiophenes such as PD81,723 and ATL525 are pos. allosteric regulators, or enhancers, of the human A1 adenosine receptor (A1AR). In equilibrium binding assays, 125I-N6-aminobenzyladenosine (125I-ABA) binds to two affinity states of A1AR with KD-high (0.33 μM) and KD-low (.apprx.10 nM). Enhancers have little effect on KD-high but convert all A1AR binding sites to the high-affinity state. Enhancers decrease the potency of guanosine 5'-O-(3-thio)triphosphate (GTPγS) as an inhibitor of agonist binding by 100-fold and increase agonist-stimulated guanine nucleotide exchange. The association of 125I-ABA to high-affinity receptors on Chinese hamster ovary (CHO)-hA1 membranes does not follow theor. single-site association kinetics but is approximated by a bi-exponential equation with t1/2 values of 1.85 and 12.8 min. Allosteric enhancers selectively increase the number of slow binding sites, possibly by stabilizing newly formed receptor-G protein complexes. A new rapid assay method scores enhancer activity on a scale from 0 to 100 based on their ability to prevent the rapid dissociation of 125I-ABA from A1AR in response to GTPγS. Compared with PD81,723, ATL525 (100 μM) scores higher (27 vs. 79) and has less antagonist activity. ATL525 functionally enhances A1 signaling to inhibit cAMP accumulation in CHO-hA1 cells. These data suggest that simultaneously binding orthosteric and allosteric enhancer ligands convert the A1AR from partly to fully coupled to G proteins and prevents rapid uncoupling upon binding of GTPγS.
IT 95523-14-1
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(allosteric enhancers of A1 adenosine receptors increase receptor-G protein coupling and counteract guanine nucleotide effects on agonist binding)
RN 95523-14-1 CAPLUS
CN Adenosine, N-[[4-amino-3-(iodo-125I)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



OSC.G 25 THERE ARE 25 CAPLUS RECORDS THAT CITE THIS RECORD (26 CITINGS)
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2002:967180 CAPLUS
DN 138:153740
TI 3'-Aminoadenosine-5'-uronamides: Discovery of the First Highly Selective Agonist at the Human Adenosine A3 Receptor
AU DeNinno, Michael P.; Masamune, Hiroko; Chenard, Lois K.; DiRico, Kenneth J.; Eller, Cynthia; Etienne, John B.; Tickner, Jeanene E.; Kennedy, Scott P.; Knight, Delvin R.; Kong, Jimmy; Oleynek, Joseph J.; Tracey, W. Ross; Hill, Roger J.
CS PGRD Groton Laboratories, Pfizer Inc., Groton, CT, 06340, USA
SO Journal of Medicinal Chemistry (2003), 46(3), 353-355
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 138:153740
GI

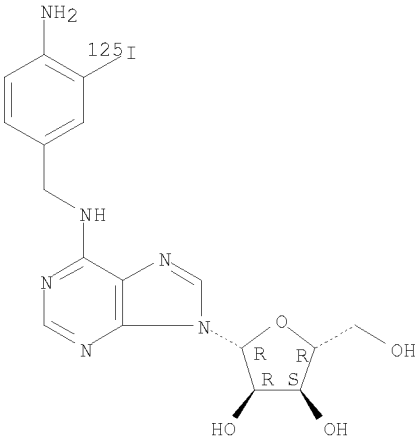


I

AB Selective adenosine A3 agonists have potential utility for the prevention of perioperative myocardial ischemic injury. Herein, we report on the discovery and synthesis of nucleoside I. This amino nucleoside agonist possesses unprecedented levels of selectivity for the human adenosine A3 receptor.
IT 95523-14-1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of 3'-aminoadenosine-5'-uronamide nucleosides as selective

agonist at the human adenosine A3 receptor)
RN 95523-14-1 CAPLUS
CN Adenosine, N-[[4-amino-3-(iodo-125I)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



OSC.G 35 THERE ARE 35 CAPLUS RECORDS THAT CITE THIS RECORD (35 CITINGS)
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2002:650986 CAPLUS
DN 137:332739
TI Structural Determinants of A3 Adenosine Receptor Activation: Nucleoside Ligands at the Agonist/Antagonist Boundary
AU Gao, Zhan-Guo; Kim, Soo-Kyung; Biadatti, Thibaud; Chen, Wangzhong; Lee, Kyeong; Barak, Dov; Kim, Seong Gon; Johnson, Carl R.; Jacobson, Kenneth A.
CS Laboratory of Bioorganic Chemistry, Molecular Recognition Section, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 20892, USA
SO Journal of Medicinal Chemistry (2002), 45(20), 4471-4484
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 137:332739
AB Mutagenesis of the human A3 adenosine receptor (AR) suggested that certain amino acid residues contributed differently to ligand binding and activation processes. Here we demonstrated that various adenosine modifications, including adenine substitution and ribose ring constraints, also contributed differentially to these processes. The ligand effects on cAMP production in intact CHO cells expressing the A3AR and in receptor binding were compared. Notably, the simple 2-fluoro group alone or 2-chloro in combination with N6-substitution dramatically diminished the efficacy of adenosine derivs., even converting agonist into antagonist. Other affinity-increasing substitutions, including N6-(3-iodobenzyl) and the (Northern)-methanocarba, also reduced efficacy, except in combination with a flexible 5'-uronamide. 2-Cl-N6-(3-iodobenzyl) derivs., both in the (N)-methanocarba (i.e., of the Northern conformation) and riboside series were potent antagonists with little residual agonism. Ring-constrained 2',3'-epoxide derivs. in both riboside and (N)-methanocarba series and a cyclized (spiral) 4',5'-uronamide derivative were synthesized and found to be human A3AR antagonists. The 4',5'-uronamide derivative bound potently at both human (26 nM) and rat (49 nM) A3ARs. A rhodopsin-based A3AR model, containing all domains except the C-terminal region, indicated sep. structural requirements for receptor binding and activation for these adenosine analogs. Ligand docking, taking into account binding of selected derivs. at mutant A3ARs, featured interactions of TM3 (His95) with the adenine moiety and TMs with the ribose 5'-region. The 5'-OH group of antagonist N6-(3-iodobenzyl)-2-chloroadenosine formed a H-bond with N274 but not with S271. The 5'-substituent of nucleoside antagonists moved toward TM7 and away from TM6. The conserved Trp243 (6.48) side chain, involved in

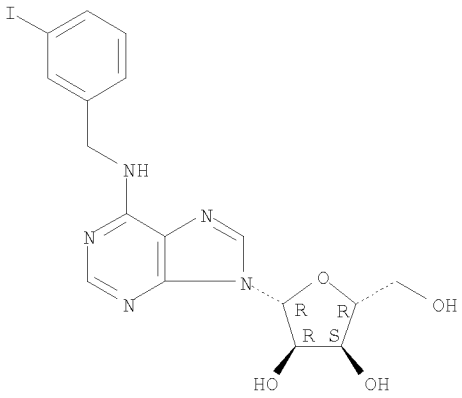
recognition of the classical (nonnucleoside) A3AR antagonists but not adenosine-derived ligands, displayed a characteristic movement exclusively upon docking of agonists. Thus, A3AR activation appeared to require flexibility at the 5'- and 3'-positions, which was diminished in (N)-methanocarba, spiro, and epoxide analogs, and was characteristic of ribose interactions at TM6 and TM7.

IT 163152-30-5
RL: PAC (Pharmacological activity); BIOL (Biological study)
(structural determinants of A3 adenosine receptor activation and nucleoside ligands at the agonist/antagonist boundary)

RN 163152-30-5 CAPLUS

CN Adenosine, N-[(3-iodophenyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



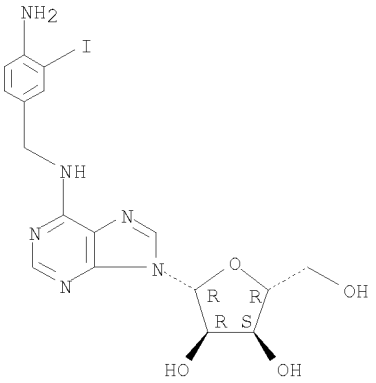
OSC.G 90 THERE ARE 90 CAPLUS RECORDS THAT CITE THIS RECORD (92 CITINGS)
RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2001:757814 CAPLUS
DN 135:298819
TI Meta-substituted acidic 8-phenylxanthine antagonists of A3 human adenosine receptors, and their therapeutic use
IN Linden, Joel M.
PA University of Virginia, USA; University of Virginia Patent Foundation
SO U.S., 16 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6303619	B1	20011016	US 1998-38991	19980312

PRAI US 1998-38991 19980312
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OS MARPAT 135:298819
AB The invention concerns the use of a xanthine or xanthine derivative having a meta-substituted acidic aryl at the 8-position to specifically modulate the physiol. role of adenosine activation of its various receptors.
IT 98866-49-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(xanthine aryl derivative antagonists of adenosine A3 receptor, and therapeutic use)
RN 98866-49-0 CAPLUS
CN Adenosine, N-[(4-amino-3-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

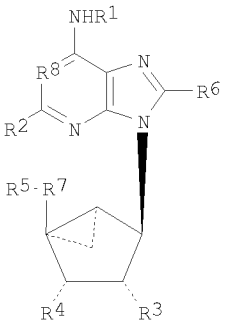


OSC.G 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
RE.CNT 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

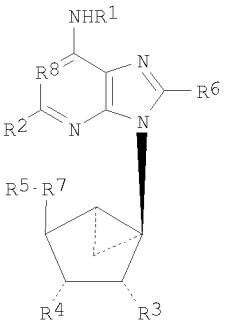
L4 ANSWER 19 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2001:526078 CAPLUS
DN 135:92808
TI Preparation of methanocarba cycloalkyl nucleoside and nucleotide analogs useful agonists or antagonists of P1 or P2 receptors
IN Jacobson, Kenneth A.; Marquez, Victor E.
PA United States Dept. of Health and Human Services, USA
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001051490	A1	20010719	WO 2001-US981	20010112
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2397366	A1	20010719	CA 2001-2397366	20010112
	AU 2001030913	A	20010724	AU 2001-30913	20010112
	EP 1252160	A1	20021030	EP 2001-903043	20010112
	EP 1252160	B1	20060816		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	AU 2001230913	B2	20050630	AU 2001-230913	20010112
	AT 336492	T	20060915	AT 2001-903043	20010112
	US 20030216412	A1	20031120	US 2002-169975	20020712
	US 7087589	B2	20060808		
	US 20060270629	A1	20061130	US 2006-500860	20060808
	US 7790735	B2	20100907		
PRAI	US 2000-176373P	P	20000114		
	WO 2001-US981	W	20010112		
	US 2002-169975	A3	20020712		

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OS MARPAT 135:92808
GI



I



II

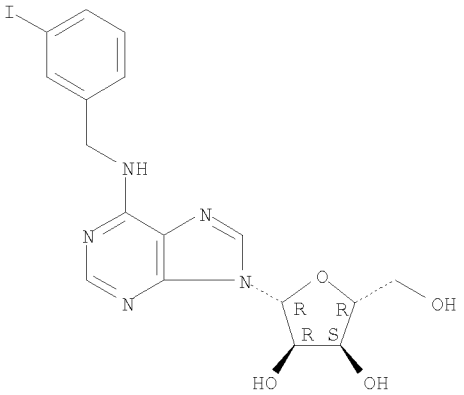
AB The present invention provides novel nucleoside and nucleotide derivs. I, wherein R1 is hydrogen, alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, arylalkyl, acyl, sulfonyl, arylsulfonyl, thiazolyl or bicyclic alkyl; R2 is hydrogen, halo, alkyl, aryl, arylamino, aryloxide, alkynyl, alkenyl, thiol, cyano, or; R3, R4–R5, are each independently hydrogen, hydroxyl, alkoxy, alkyl, alkenyl, alkynyl, aryl, acyl, alkylamino, arylamino, phosphoryl, diphosphoryl, triphosphoryl, phosphonyl, boronyl, thiophosphoryl, thiodiphosphoryl, thiotriphosphoryl or vanadyl, and can be the same or different; R6 is hydrogen, alkyl, alkenyl, alkynyl, heteroaryl or aminoalkyl; R7 is methylene, dihalomethyl, carbonyl, sulfoxide; and at least one of R1, R2, and R6. is other than hydrogen; R8 is carbon or nitrogen; that are useful agonists or antagonists of P1 or P2 receptors. For example, the present invention provides a compound of formula A–M, wherein A is modified adenine or uracil and M is a constrained cycloalkyl group. The adenine or uracil is bonded to the constrained cycloalkyl group. The compds. of the present invention are useful in the treatment or prevention of various diseases including airway diseases (through A2B, A3, P2Y2 receptors), cancer (through A3, P2 receptors), cardiac arrhythmias (through A1 receptors), cardiac ischemia (through A1, A3 receptors), epilepsy (through A1, P2X receptors), and Huntington's Disease (through A2A receptors). Thus, (N)–Methanocarba–N6–methyl–2–chloro–2'–deoxyadenosine–3,5'–bis(diammonium phosphate) was prepared and tested as agonists or antagonists of P1 or P2 receptor. In binding assays at A1, A2A, and A3 receptors, N–methanocarba–adenosine proved to be of higher affinity than the S–analog, with an N:S–conformation affinity ratio of 150 at the human A3 receptor. Thus, the biol. potency and efficacy of this series of nucleosides appears to be highly dependent on ring puckering, which in turn would influence the orientation of the hydroxyl groups within the receptor binding site. The structure activity relationship (SAR) of adenosine agonists indicates that the ribose ring oxygen may be substituted with carbon. N–Methanocarba N6–(3–iodobenzyl)adenosine and the 2–chloro derivative had Ki values of 4.1 and 2.2 nM at A3 receptors, resp., and were selective partial agonists.

IT 163152–30–5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of methanocarba cycloalkyl nucleoside and nucleotide analogs useful agonists or antagonists of p or p receptors)

RN 163152–30–5 CAPLUS

CN Adenosine, N–[(3–iodophenyl)methyl]– (CA INDEX NAME)

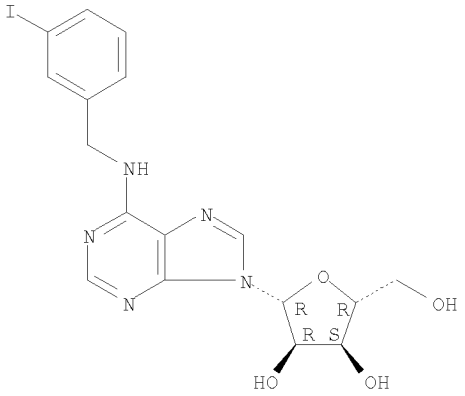
Absolute stereochemistry.



OSC.G 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2000:316191 CAPLUS
DN 133:83860
TI Methanocarba Analogues of Purine Nucleosides as Potent and Selective Adenosine Receptor Agonists
AU Jacobson, Kenneth A.; Ji, Xiao-duo; Li, An-Hu; Melman, Neli; Siddiqui, Maqbool A.; Shin, Kye-Jung; Marquez, Victor E.; Ravi, R. Gnana
CS Molecular Recognition Section Laboratory of Bioorganic Chemistry National Institute of Diabetes Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892-0810, USA
SO Journal of Medicinal Chemistry (2000), 43(11), 2196-2203
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB Adenosine receptor agonists have cardioprotective, cerebroprotective, and antiinflammatory properties. The authors report that a carbocyclic modification of the ribose moiety incorporating ring constraints is a general approach for the design of A1 and A3 receptor agonists having favorable pharmacodynamic properties. While simple carbocyclic substitution of adenosine agonists greatly diminishes potency, methanocarba-adenosine analogs have now defined the role of sugar puckering in stabilizing the active adenosine receptor-bound conformation and thereby have allowed identification of a favored isomer. In such analogs a fused cyclopropane moiety constrains the pseudosugar ring of the nucleoside to either a Northern (N) or Southern (S) conformation, as defined in the pseudorotational cycle. In binding assays at A1, A2A, and A3 receptors, (N)-methanocarba-adenosine was of higher affinity than the (S)-analog, particularly at the human A3 receptor (N/S affinity ratio of 150). (N)-methanocarba analogs of various N6-substituted adenosine derivs., including cyclopentyl and 3-iodobenzyl, in which the parent compds. are potent agonists at either A1 or A3 receptors, resp., were synthesized. The N6-cyclopentyl derivs. were A1 receptor-selective and maintained high efficacy at recombinant human but not rat brain A1 receptors, as indicated by stimulation of binding of [35S]GTP-γ-S. The (N)-methanocarba-N6-(3-iodobenzyl)adenosine and its 2-chloro derivative had Ki values of 4.1 and 2.2 nM at A3 receptors, resp., and were highly selective partial agonists. Partial agonism combined with high functional potency at A3 receptors (EC50 < 1 nM) may produce tissue selectivity. In conclusion, as for P2Y1 receptors, at least three adenosine receptors favor the ribose (N)-conformation.
IT 163152-30-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(methanocarba analogs of purine nucleosides as potent and selective adenosine receptor agonists)
RN 163152-30-5 CAPLUS
CN Adenosine, N-[(3-iodophenyl)methyl]- (CA INDEX NAME)

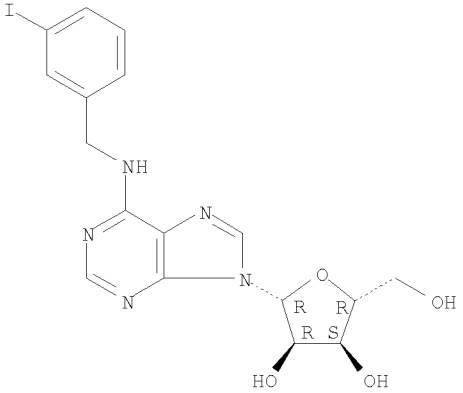
Absolute stereochemistry.



OSC.G 85 THERE ARE 85 CAPLUS RECORDS THAT CITE THIS RECORD (86 CITINGS)
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 1999:205653 CAPLUS
DN 130:282291
TI N6,5'-Disubstituted Adenosine Derivatives as Partial Agonists for the Human Adenosine A3 Receptor
AU Van Tilburg, Erica W.; von Kuenzel, Jacobien; de Groote, Miriam; Vollinga, Roel C.; Lorenzen, Anna; IJzerman, Ad P.
CS Division of Medicinal Chemistry, Leiden/Amsterdam Center for Drug Research, Leiden, 2300 RA, Neth.
SO Journal of Medicinal Chemistry (1999), 42(8), 1393-1400
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB 5'-(Alkylthio)-substituted analogs of N6-benzyl- and N6-(3-iodobenzyl)adenosine were synthesized in 37-61% overall yields. The affinities of these compds. for the adenosine A1, A2a, and A3 receptors were determined using rat brain cortex, rat brain striata, and stably transfected human A3 receptors in HEK 293 cells, resp. The compds. proved to be selective for the adenosine A3 receptor and displayed affinities in the nanomolar range. Three compds. had the highest affinities for the A3 receptor with Ki values ranging from 8.8 to 27.7 nM. In the N6-benzyl series, compound LUF 5403, with a 5'-methylthio group, maintained a reasonable affinity and had the highest selectivity for the A3 receptor. Compound LUF 5411, with an N6-(3-iodobenzyl) group and a 5'-(n-propylthio) substituent, had the highest A3 selectivity of all of the compds. and also displayed high affinity for this receptor (Ki = 44.3 nM). The compds. were also evaluated for their ability to stimulate [35S]GTPγ[S] binding in cell membranes expressing the human adenosine A3 receptor. It appeared that the N6,5'-disubstituted adenosine derivs. behaved as partial agonists. Four compds. had very high intrinsic activities; addnl., when tested in a cAMP assay, these compds. also behaved as partial agonists.
IT 163152-30-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of N6,5'-disubstituted adenosine derivs. as partial agonists for the human adenosine A3 receptor)
RN 163152-30-5 CAPLUS
CN Adenosine, N-[(3-iodophenyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.

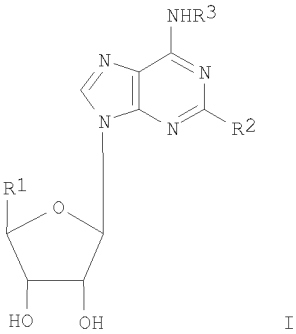


OSC.G 40 THERE ARE 40 CAPLUS RECORDS THAT CITE THIS RECORD (40 CITINGS)
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 1998:441960 CAPLUS
DN 129:109311
OREF 129:22461a,22464a
TI Preparation of nucleoside uronamides as A3 adenosine receptor agonists
IN Jacobson, Kenneth A.; Gallo-Rodriguez, Carola; Van Galen, Philip J. M.; Von Lubitz, Dag K. J. E.; Jeong, Heaok Kim
PA United States Dept. of Health and Human Services, USA
SO U.S., 54 pp., Cont.-in-part of U. S. Ser. No. 163,324, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5773423	A	19980630	US 1994-274628	19940713
	US 5688774	A	19971118	US 1995-396111	19950228
PRAI	US 1993-91109	B2	19930713		
	US 1993-163324	B2	19931206		
	US 1994-274628	A2	19940713		

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OS MARPAT 129:109311
GI



I

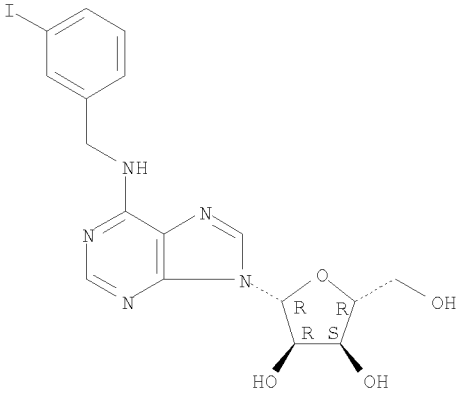
AB The present invention provides N6-benzyladenosine-5'-N-uronamide and related substituted compds. I (R1 = amide; R2 = halo, amino, alkenyl, alkynyl, thio, alkylthio; R3 = S-1-phenylethyl, Bn, phenylethyl), particularly those containing substituents on the benzyl and/or uronamide groups, and modified xanthine ribosides, as well as pharmaceutical compns.

containing such compds. The present invention also provides a method of selectively activating an A3 adenosine receptor in a mammal, which method comprises acutely or chronically administering to a mammal in need of selective activation of its A3 adenosine receptor a therapeutically effective amount of a compound which binds with the A3 receptor so as to stimulate an A3 receptor-dependent response. Thus, N6-(3-iodobenzyl)adenosine was prepared tested for its affinity in binding at rat brain A1, A2, A3 adenosine receptors (Ki = 9.5-220.0 nM).

IT 163152-30-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nucleoside uronamides as A3 adenosine receptor agonists)

RN 163152-30-5 CAPLUS
CN Adenosine, N-[(3-iodophenyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.

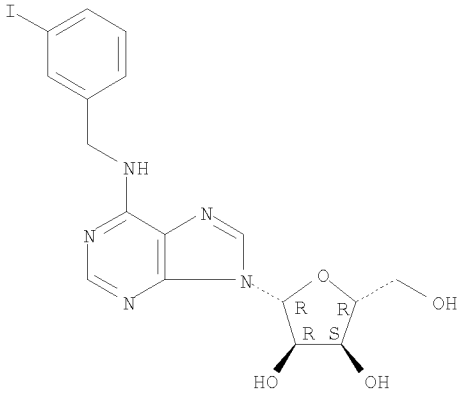


OSC.G 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 1998:329095 CAPLUS
DN 129:75990
OREF 129:15525a,15528a
TI A functional screening of adenosine analogs at the adenosine A2B receptor: a search for potent agonists
AU De Zwart, Maarten; Link, Regina; Von Frijtag Drabbe Kunzel, Jacobien K.; Cristalli, Gloria; Jacobson, Kenneth A.; Townsend-Nicholson, Andrea; Ijzerman, Ad P.
CS Division of Medicinal Chemistry, Leiden/Amsterdam Center for Drug Research, Leiden University, Leiden, 2300 RA, Neth.
SO Nucleosides & Nucleotides (1998), 17(6), 969-985
CODEN: NUNUD5; ISSN: 0732-8311
PB Marcel Dekker, Inc.
DT Journal
LA English
AB Various adenosine analogs were tested at the adenosine A2B receptor. Agonist potencies were determined by measuring the cAMP production in Chinese Hamster Ovary cells expressing human A2B receptors. 5'-N-Substituted carboxamidoadenosines were most potent. 5'-N-Ethylcarboxamidoadenosine (NECA) was most active with an EC50 value of 3.1 μM. Other ribose modified derivs. displayed low to negligible activity. Potency was reduced by substitution on the exocyclic amino function (N6) of the purine ring system. The most active N6-substituted derivative N6-methyl-NECA was 5 fold less potent than NECA. C8- and most C2-substituted analogs were virtually inactive. 1-Deaza-analogs had a reduced potency, 3- and 7-deazaanalogues were not active.
IT 163152-30-5
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(functional screening of adenosine analogs at adenosine A2B receptor:

search for potent agonists)
RN 163152-30-5 CAPLUS
CN Adenosine, N-[(3-iodophenyl)methyl]- (CA INDEX NAME)

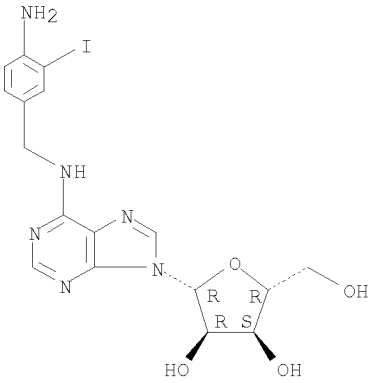
Absolute stereochemistry.



OSC.G 45 THERE ARE 45 CAPLUS RECORDS THAT CITE THIS RECORD (46 CITINGS)
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 1997:803243 CAPLUS
DN 128:84646
OREF 128:16405a,16408a
TI Inosine binds to A3 adenosine receptors and stimulates mast cell degranulation
AU Jin, Xiaowei; Shepherd, Rebecca K.; Duling, Brian R.; Linden, Joel
CS Department of Biochemistry, University of Virginia Health Sciences Center, Charlottesville, VA, 22908, USA
SO Journal of Clinical Investigation (1997), 100(11), 2849-2857
CODEN: JCINAO; ISSN: 0021-9738
PB Rockefeller University Press
DT Journal
LA English
AB The authors investigated the mechanism by which inosine, a metabolite of adenosine that accumulates to >1 mM levels in ischemic tissues, triggers mast cell degranulation. Inosine was found to do the following: (a) compete for [125I]N6-aminobenzyladenosine binding to recombinant rat A3 adenosine receptors (A3AR) with an IC50 of 25±6 μM; (b) not bind to A1 or A2A ARs; (c) bind to newly identified A3ARs in guinea pig lung (IC50 = 15±4 μM); (d) lower cAMP in HEK-293 cells expressing rat A3ARs (ED50 = 12±5 μM); (e) stimulate RBL-2H3 rat mast-like cell degranulation (ED50 = 2.3±0.9 μM); and (f) cause mast cell-dependent constriction of hamster cheek pouch arterioles that is attenuated by A3AR blockade. Inosine differs from adenosine in not activating A2AARs that dilate vascular smooth muscle and inhibit mast cell degranulation. The A3 selectivity of inosine may explain why it elicits a monophasic arteriolar constrictor response distinct from the multiphasic dilator/constrictor response to adenosine. Nucleoside accumulation and an increase in the ratio of inosine to adenosine may provide a physiol. stimulus for mast cell degranulation in ischemic or inflamed tissues.
IT 98866-49-0
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(inosine binds to A3 adenosine receptors and stimulates mast cell degranulation in tissue culture)
RN 98866-49-0 CAPLUS
CN Adenosine, N-[(4-amino-3-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



OSC.G 118 THERE ARE 118 CAPLUS RECORDS THAT CITE THIS RECORD (118 CITINGS)
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 1996:701996 CAPLUS
DN 126:1192
OREF 126:275a,278a
TI Methods for protecting tissues and organs from ischemic damage
IN Downey, James M.; Mullane, Kevin M.
PA Gensia, Inc., USA; South Alabama Medical Science Foundation
SO U.S., 16 pp., Cont.-in-part of U.S. 5, 443, 836.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

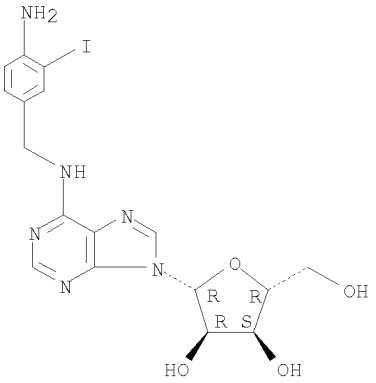
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5573772	A	19961112	US 1994-214942	19940317
	US 5443836	A	19950822	US 1993-33310	19930315
PRAI	US 1993-33310	A2	19930315		

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Methods for protecting tissues and organs including the heart central nervous system, and kidney from ischemic damage are described and claimed based upon the recognition that protection against infarction is mediated by A3 rather than A1 adenosine receptors, as was previously thought, and that the receptor mediating protection in other organs and tissues has not been defined. Methods for selectively stimulating A3 adenosine receptors are described and claimed, as such selection is shown to prevent or substantially reduce cell death resulting from ischemia with or without reperfusion in humans. According to this invention, the A3 adenosine receptor is selectively stimulated by administering a compound which is an A3 adenosine receptor-selective agonist. Prevention of tissue death is also achieved by administering a compound which is a non-selective adenosine receptor agonist together with compds. that act as antagonists to the A1 and A2 adenosine receptor.

IT 98866-49-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for protecting tissues and organs from ischemic damage)
RN 98866-49-0 CAPLUS
CN Adenosine, N-[(4-amino-3-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

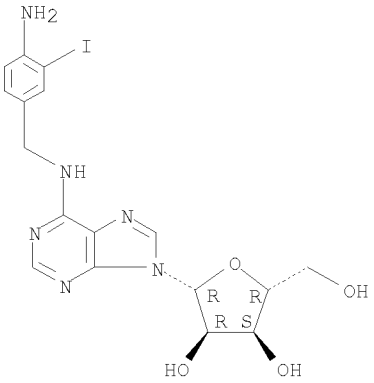
Absolute stereochemistry.



OSC.G 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 26 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 1996:252943 CAPLUS
DN 124:308239
OREF 124:56903a,56906a
TI Inhibition of TNF-α expression by adenosine. Role of A3 adenosine receptors
AU Sajjadi, Fereydoun G.; Takabayashi, Ken; Foster, Alan C.; Domingo, Ron C.; Firestein, Gary S.
CS Gensia, Inc., San Diego, CA, 92121, USA
SO Journal of Immunology (1996), 156(9), 3435-42
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB Adenosine agonists inhibit TNF-α production in macrophage and monocytes, but the mechanism is unknown. Therefore, we studied the human macrophage cell line U937 to determine the adenosine receptor subtypes responsible and the intracellular signaling mechanisms involved. The A1/A3 agonist N6-(4-amino-3-iodobenzyl)adenosine (I-ABA) decreased LPS-stimulated TNF-α protein production by 79%. The mechanism was pretranslational, as adenosine receptor stimulation caused a marked decrease in TNF-α mRNA. IL-1β, IL-6, and IL-8 mRNA were not changed by adenosine agonists. The rank order of agonists as TNF-α inhibitors suggested that the A3 receptor might be involved (N6-(3-iodobenzyl)-9-[5-(methylcarbamoyl)-β-D-ribofuranosyl]adenosine > 2-chloroadenosine ≥ I-ABA > N6-benzyl-5'-N-ethylcarboxamidoadenosine > NECA > CGS21680 > N6-cyclohexyladenosine), and this was supported by the fact that a mixed A1/A3 antagonist (xanthine amine congener) reversed the effect, whereas A1-specific (1,3-dipropyl-8-cyclopentylxanthine) and A2-specific (3,7-dimethyl-1-propargylxanthine) antagonists did not. Receptor signaling did not involve cAMP or protein kinase A, nor did it alter the activation and binding characteristics of the transcription factor NF-κB. However, the composition of the AP-1 transcription complex was altered by I-ABA. These data suggest that stimulation of the A3 adenosine receptor can alter the cytokine milieu by decreasing TNF-α. Adenosine agonists or adenosine regulating agents have potential therapeutic uses in acute and chronic inflammatory diseases.
IT 98866-49-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(adenosine inhibition of TNF-α expression by human macrophage cell line mediation by A3 receptors)
RN 98866-49-0 CAPLUS
CN Adenosine, N-[(4-amino-3-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



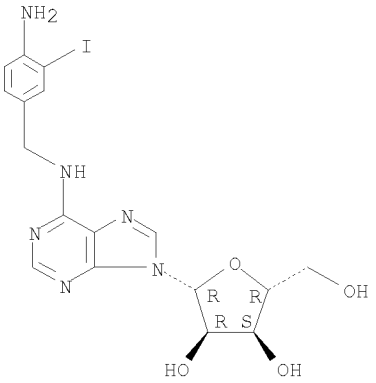
OSC.G 267 THERE ARE 267 CAPLUS RECORDS THAT CITE THIS RECORD (268 CITINGS)

L4 ANSWER 27 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 1996:52783 CAPLUS
DN 124:194308
OREF 124:35679a
TI Xanthine-derived A3 adenosine receptor subtype-specific antagonists for alteration of eosinophil cytokine-induced hypersensitivity
IN Jacobson, Marlene A.; Johnson, Robert G.; Salvatore, Christopher A.
PA Merck and Co., Inc., USA
SO Brit. UK Pat. Appl., 96 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 2288733	A	19951101	GB 1995-7984	19950419
US 5646156	A	19970708	US 1994-233009	19940425
PRAI US 1994-233009	A	19940425		

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OS MARPAT 124:194308
AB There are described A3-adenosine receptor subtype-specific antagonists (especially xanthine derivs.) which, when contacted with eosinophils, have at least one of the following effects on the biol. properties of the eosinophil: (1) decrease in intracellular cAMP; (2) blockage of activation; (3) prevention of A3 adenosine receptor subtype inhibition of adenylate cyclase; (4) blockage of cytokine-induced hypersensitivity. The antagonists may be used in the therapy of allergic and inflammatory states. There are also disclosed nucleic acid sequences for use as an in situ hybridization probe, or as a primer for reverse transcriptase polymerase chain reaction anal. in the identification of a specific adenosine receptor subtype.
IT 98866-49-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(xanthine-derived A3 adenosine receptor subtype-specific antagonists for alteration of eosinophil cytokine-induced hypersensitivity)
RN 98866-49-0 CAPLUS
CN Adenosine, N-[(4-amino-3-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

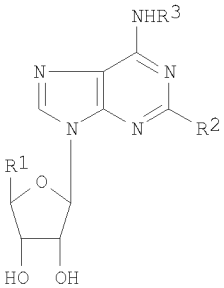


OSC.G 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

L4 ANSWER 28 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 1995:837438 CAPLUS
DN 123:257265
OREF 123:46034h,46035a
TI Preparation of N6-benzyladenosine-5'-uronamides, modified xanthine ribosides, and related compounds as adenosine A3 receptor agonists.
IN Jacobson, Kenneth A.; Gallo-Rodriguez, Carola; Von Galen, Philip J. M.; Von Lubitz, Dag K. J. E.; Jeong, Heaok Kim
PA United States Dept. of Health and Human Services, USA
SO PCT Int. Appl., 175 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9502604	A1	19950126	WO 1994-US7835	19940713
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9473310	A	19950213	AU 1994-73310	19940713
	EP 708781	A1	19960501	EP 1994-923445	19940713
	EP 708781	B1	20011004		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	AT 206432	T	20011015	AT 1994-923445	19940713
PRAI	US 1993-91109	A	19930713		
	US 1993-163324	A	19931206		
	WO 1994-US7835	W	19940713		

OS MARPAT 123:257265
GI



I

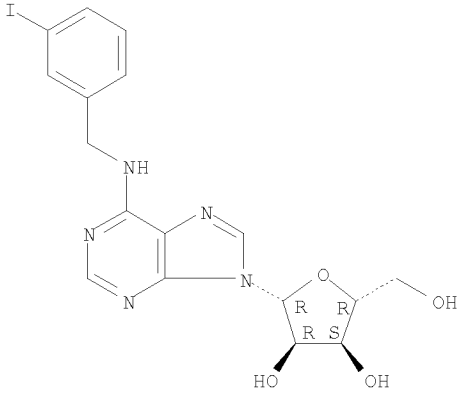
AB Title compds. [I; R1 = RaRbNCO, HORc; Ra, Rb = H, alkyl, amino, haloalkyl, aminoalkyl, cycloalkyl, BOC-aminoalkyl; RaRbN = heterocyclyl; Rc = alkyl, amino, haloalkyl, aminoalkyl, cycloalkyl, BOC-aminoalkyl; R2 = H, halo,

alkyl ether residue, amino, alkylamino, alkenyl, alkynyl, thio, alkylthio; R3 = (R)- and (S)-1-phenylethyl, (substituted) PhCH2, substituted phenylethyl] and related compds., were prepared Thus, 2-chloro-N6-(3-iodobenzyl)adenine was refluxed with hexamethyldisilazane and cat. (NH4)2SO4 to give a silyl derivative which was refluxed with N-Me I-O-acetyl-2,3-dibenzoyl-α,β-D-ribofuronamide and trimethylsilyl triflate in dichloroethane to give 2-chloro-N6-(3-iodobenzyl)-9-[5-(methylamido)-2,3-di-O-benzoyl-β-D-ribofuranosyl]adenine. The latter was stirred with NH3 in MeOH for 16 h to give 68.7% 2-chloro-N6-(3-iodobenzyl)-9-[5-(methylamido)-β-D-ribofuranosyl]adenine. This showed Ki = 0.23 nM in a radioligand binding assay at rat brain A3 receptors.

IT 163152-30-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N6-benzyladenosine-5'-uronamides, modified xanthine ribosides, and related compds. as adenosine A3 receptor agonists)

RN 163152-30-5 CAPLUS
CN Adenosine, N-[(3-iodophenyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



OSC.G 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 29 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 1995:833970 CAPLUS
DN 123:247385
OREF 123:43971a,43974a
TI The human A1 adenosine receptor: ligand binding properties, sites of somatic expression and chromosomal localization
AU Rivkees, Scott A.; Lasbury, Mark E.; Stiles, Gary S.; Henegariu, Octavian; Curtis, Christine; Vance, Gail
CS Section of Pediatric Endocrinology, Indiana University Medical School, Indianapolis, IN, 46202, USA
SO Endocrine (1995), 3(9), 623-9
CODEN: EOCRE5; ISSN: 1355-008X
PB Macmillan Scientific & Medical Division
DT Journal
LA English
AB The A1 adenosine receptor (A1AR) exerts import biol. effects in the mammalian biol. To provide insights into the role A1AR action in human physiol., the authors characterized the pharmacol. properties of the human A1AR, examined somatic sites of A1AR gene expression, and identified the chromosomal location of the human A1AR gene. Using stably transfected CHO cells, the ligand binding properties of human and rat A1ARs were directly compared. Saturation studies showed that the human and rat A1ARs had similar high affinity for the A1 agonist [3H]CCPA (human, Kd = 517 pM; Bmax 438 fmol/mg of protein; rat, Kd = 429 pM; Bmax 358 fmol/mg of protein). Competition studies performed using seven adenosine agonists and four adenosine antagonists also did not detect differences in the ligand binding properties among the rat and human A1ARs. Northern anal. of 16

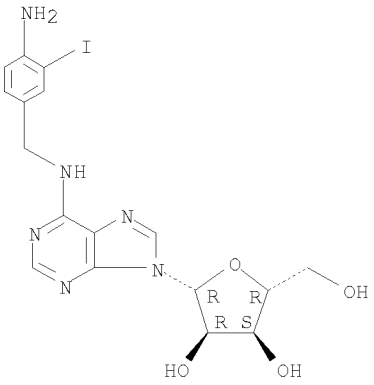
human tissues revealed the presence of a single hybridizing transcript of 2.5 kb. Human A1AR receptor mRNA expression was greatest in brain and testis; lower levels of A1AR mRNA were present in heart, pancreas, kidney and spleen. Southern blotting and PCR anal. of human-rodent somatic cell hybrids showed that the A1AR gene is on human chromosome 1. Using fluorescence in situ hybridization, the human A1AR gene was further localized to the 1q32.1 region. These observations show that the human A1AR is a high affinity receptor that has ligand binding properties similar to the rat A1AR, human A1AR mRNA is heavily expressed in brain and testis, and the gene encoding the human A1AR is present on the long arm of chromosome 1.

IT 98866-49-0
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ligand binding properties, sites of somatic expression and chromosomal localization of the human A1 adenosine receptor)

RN 98866-49-0 CAPLUS

CN Adenosine, N-[(4-amino-3-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



OSC.G 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

L4 ANSWER 30 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN

AN 1995:708692 CAPLUS

DN 123:208767

OREF 123:36987a,36990a

TI Human adenosine receptor antagonists

IN Doyle, Michael P.; Jacobson, Marlene A.; Duling, Brian R.; Johnson, Robert G.; Linden, Joel M.

PA Merck and Co., Inc., USA; University of Virginia Patents Foundation

SO PCT Int. Appl., 108 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9511681	A1	19950504	WO 1994-US12272	19941026
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRAI US 1993-145437	A	19931029		

OS MARPAT 123:208767

AB Compds. are identified through the use of recombinant human adenosine receptors A1, A2a, A2b, and A3, which specifically modulate the physiol. role of adenosine activation of its various receptors. In particular, a method is describing for achieving specific blockage of the A3 subtype of the adenosine receptor, and xanthines and xanthine derivs are described which display potent and specific A3-subtype specificity. Thus, full-length cDNAs were isolated and sequenced encoding the A1, A2a, A2b, and A3 receptors; these cDNAs were used in constructs for cloning expression in COS, CHO, and HEK 293 cells. The human A3 adenosine receptor cDNA encodes for a protein of 318 amino acids and exhibits 72 and 85% overall identity with the rat and sheep A3 adenosine receptor

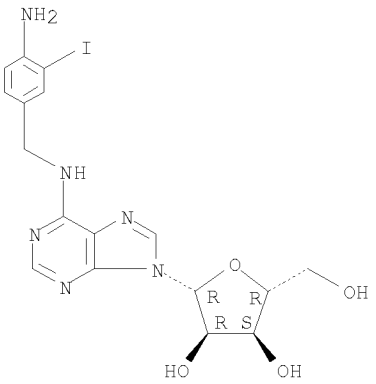
sequences, resp. Specific and saturable binding of the receptor agonist 125I-N6-aminobenzyladenosine was measured on the human A3 receptor stably expressed in CHO cells with a KD of 10 nM. The potency order or adenosine receptor agonists was determined to be N-ethylcarboxamidoadenosine ≥ R-phenylisopropyladenosine > N6-cyclopentyladenosine > S-phenylisopropyladenosine. The human receptor was blocked by xanthine antagonists; a partial listing of the pharmacol. is that the potency order of antagonists is I-ABOPX > 1,3-dipropyl-8-(4-acrylate) phenylxanthine (BW-A1433) ≥ xanthine amino congener (XAC) >> 1,3-dipropyl-8-0cyclopentylxanthine. Antagonist potencies determined by Schild analyses correlated well with those established by competition for radioligand binding. The tissue distribution of transcripts for all of the human adenosine receptor subtypes was compared. Compds. identified as antagonists are useful in preventing mast cell degranulation and are therefore useful in the treatment or prevention of disease states induced by activation of the A3 receptor and mast cell activation. These disease states include asthma, myocardial reperfusion injury, and allergic reactions including rhinitis, poison ivy-induced responses, urticaria, scleroderma, arthritis, other autoimmune diseases, and inflammatory bowel diseases.

IT 98866-49-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human adenosine receptor antagonists)

RN 98866-49-0 CAPLUS

CN Adenosine, N-[(4-amino-3-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



OSC.G 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

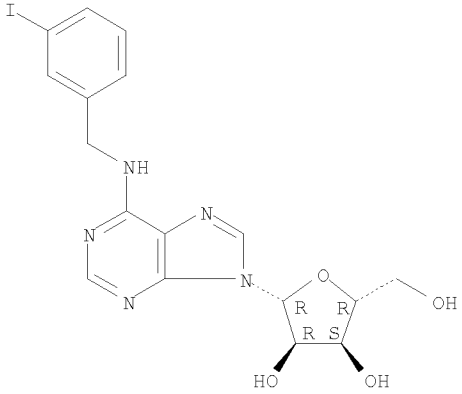
L4 ANSWER 31 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 1995:55075 CAPLUS
DN 122:291402
OREF 122:53147a,53150a
TI 2-Substitution of N6-Benzyladenosine-5'-uronamides Enhances Selectivity for A3 Adenosine Receptors
AU Kim, Hea O.; Ji, Xiao-duo; Siddiqi, Suhaib M.; Olah, Mark E.; Stiles, Gary L.; Jacobson, Kenneth A.
CS Laboratory of Bioorganic Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 20892, USA
SO Journal of Medicinal Chemistry (1994), 37(21), 3614-21
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
AB Adenosine derivs. bearing an N6-(3-iodobenzyl) group, reported to enhance the affinity of adenosine-5'-uronamide analogs as agonists at A3 adenosine receptors, were synthesized starting from Me β-D-ribofuranoside in 10 steps. Binding affinities at A1 and A2a receptors in rat brain membranes and at cloned rat A3 receptors from stably transfected CHO cells were compared. N6-(3-Iodobenzyl)adenosine was 2-fold selective for A3 vs A1 or

A2a receptors; thus it is the first monosubstituted adenosine analog having any A3 selectivity. The effects of 2-substitution in combination with modifications at the N6- and 5'-positions were explored. 2-Chloro-N6-(3-iodobenzyl)adenosine had a Ki value of 1.4 nM and moderate selectivity for A3 receptors. 2-Chloro-N6-(3-iodobenzyl)adenosine-5'-N-methyluronamide, which displayed a Ki value of 0.33 nM, was selective for A3 vs A1 and A2a receptors by 2500- and 1400-fold, resp. It was 46,000-fold selective for A3 receptors vs the Na+-independent adenosine transporter, as indicated in displacement of [3H]N6-(4-nitrobenzyl)thioinosine binding in rat brain membranes. In a functional assay in CHO cells, it inhibited adenylate cyclase via rat A3 receptors with an IC50 of 67 nM. 2-(Methylthio)-N6-(3-iodobenzyl)adenosine-5'-N-methyluronamide and 2-(methylamino)-N6-(3-iodobenzyl)adenosine-5'-N-methyluronamide were less potent, but nearly as selective for A3 receptors. Thus, 2-substitution (both small and sterically bulky) is well-tolerated at A3 receptors, and its A3 affinity-enhancing effects are additive with effects of uronamides at the 5'-position and a 3-iodobenzyl group at the N6-position.

IT 163152-30-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of iodobenzyladenosine uronamides and binding affinities at adenosine receptors)

RN 163152-30-5 CAPLUS
CN Adenosine, N-[(3-iodophenyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



OSC.G 136 THERE ARE 136 CAPLUS RECORDS THAT CITE THIS RECORD (136 CITINGS)

L4 ANSWER 32 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 1994:125921 CAPLUS
DN 120:125921
OREF 120:22025a,22028a
TI Molecular cloning and functional expression of a sheep A3 adenosine receptor with widespread tissue distribution
AU Linden, Joel; Taylor, Heidi E.; Robeva, Anna S.; Tucker, Amy L.; Stehle, Jorg H.; Rivkees, Scott A.; Fink, J. Stephen; Reppert, Steven M.
CS Lab. Dev. Chronobiol., Massachusetts Gen. Hosp., Boston, MA, 02114, USA
SO Molecular Pharmacology (1993), 44(3), 524-32
CODEN: MOPMA3; ISSN: 0026-895X
DT Journal
LA English
AB Using the polymerase chain reaction, an A3 adenosine receptor has been cloned from the hypophysial par tuberalis of sheep. The clone encodes a 317-amino acid protein that is 72% identical to the rat A3 adenosine receptor. In contrast to rat, where abundant A3 mRNA transcript is found primarily in testis, the sheep transcript is most abundant in lung, spleen, and pineal gland and is present in moderate levels in brain, kidney, and testis. The agonist N6-amino[125I]iodobenzyladenosine binds with high affinity (Kd .simeq. 6 nM) and specificity to recombinant A3 adenosine receptors expressed transiently in COS-1 cells or stably in CHO K1 cells. The potency order of agonists is N6-aminoiodobenzyladenosine >

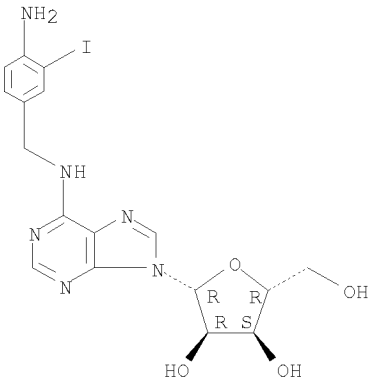
N-ethylcarboxamidoadenosine ≥ (R)-phenylisopropyladenosine » cyclopentyladenosine. Little or no binding of purine nucleotides was detected. The potency order of antagonists is 3-(3-iodo-4-aminobenzyl)-8-(4-oxyacetate)phenyl-1-propylxanthine (I-ABOPX) (Ki = 3 nM) > 1,3-dipropyl-8-(4-acrylate)phenylxanthine (BW-A1433) > 1,3-dipropyl-8-sulfophenylxanthine = xanthine amine congener » 8-cyclopentyl-1,3-dipropylxanthine. Enprofylline does not bind. These data indicate that, in contrast to A1 adenosine receptors, A3 adenosine receptors preferentially bind ligands with aryl rings in the N6-position of adenine and in the C8-position of xanthine. Among antagonists, the A3 adenosine receptor preferentially binds 8-phenylxanthines with acidic vs. basic para-substituents (I-ABOPX > BW-A1433 > 1,3-dipropyl-8-sulforphenylxanthine = xanthine amine congener). Agonists reduce forskolin-stimulated cAMP accumulation in Chinese hamster ovary cells stably transfected with recombinant sheep A3 adenosine receptors; the reduction is blocked by BW-A1433 but not by 8-cyclopentyl-1,3-dipropylxanthine. These data suggest that (i) A3 adenosine receptors display unusual structural diversity for species homologs, (ii) in contrast to rat, sheep A3 adenosine receptors have a broad tissue distribution, and (iii) some xanthines with acidic side chains bind with high affinity to A3 adenosine receptors.

IT 98866-49-0
RL: BIOL (Biological study)
(binding to sheep A3 adenosine receptor of)

RN 98866-49-0 CAPLUS

CN Adenosine, N-[(4-amino-3-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



OSC.G 137 THERE ARE 137 CAPLUS RECORDS THAT CITE THIS RECORD (140 CITINGS)

L4 ANSWER 33 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN

AN 1994:96594 CAPLUS

DN 120:96594

OREF 120:16995a,16998a

TI Molecular cloning and characterization of the human A3 adenosine receptor

AU Salvatore, Christopher A.; Jacobson, Marlene A.; Taylor, Heidi E.; Linden, Joel; Johnson, Robert G.

CS Dep. Pharmacol., Merck Res. Lab., West Point, PA, 19486, USA

SO Proceedings of the National Academy of Sciences of the United States of America (1993), 90(21), 10365-9
CODEN: PNASA6; ISSN: 0027-8424

DT Journal

LA English

AB The human A3 adenosine receptor was cloned from a striatal cDNA library using a probe derived from the homologous rat sequence. The cDNA encodes a protein of 318 amino acids and exhibits 72% and 85% overall identity with the rat and sheep A3 adenosine receptor sequences, resp. Specific and saturable binding of the adenosine receptor agonist N6-(4-amino-3-[125I]iodobenzyl)adenosine [125I]ABA was measured on the human A3 receptor stably expressed in Chinese hamster ovary cells with a Kd = 10 nM. The potency order for adenosine receptor agonists was N-ethylcarboxamidoadenosine (NECA) ≥ (R)-N6-phenyl-2-propyladenosine [(R)-PIA] > N6-cyclopentyladenosine (CPA)

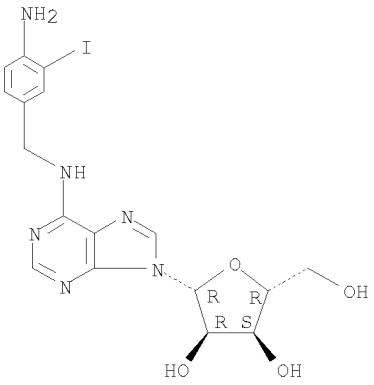
> (S)-N6-phenyl-2-propyladenosine [(S)-PIA]. The human receptor was blocked by xanthine antagonists, most potently by 3-(3-iodo-4-aminobenzyl)-8-(4-oxyacetate)phenyl-1-propylxanthine (I-ABOPX) with a potency order of I-ABOPX > 1,3-dipropyl-8-(4-acrylate)phenylxanthine ≥ xanthine amino congener >> 1,3-dipropyl-8-cyclopentylxanthine. Adenosine, NECA, (R)- and (S)-PIA, and CPA inhibited forskolin-stimulated cAMP accumulation by 30-40% in stably transfected cells; I-ABA is a partial agonist. When measured in the presence of antagonists, the dose-response curves of NECA-induced inhibition of forskolin-stimulated cAMP accumulation were right-shifted. Antagonist potencies determined by Schild analyses correlated well with those established by competition for radioligand binding. The A3 adenosine receptor transcript is widespread and, in contrast to the A1, A2a, and A2b transcripts, the most abundant expression is found in the lung and liver. The tissue distribution of A3 mRNA is more similar to the widespread profile found in sheep than to the restricted profile found in the rat. This raises the possibility that numerous physiol. effects of adenosine may be mediated by A3 adenosine receptors.

IT 98866-49-0
RL: BIOL (Biological study)
(human A3 adenosine receptor binding affinity for)

RN 98866-49-0 CAPLUS

CN Adenosine, N-[(4-amino-3-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



OSC.G 254 THERE ARE 254 CAPLUS RECORDS THAT CITE THIS RECORD (255 CITINGS)

L4 ANSWER 34 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN

AN 1993:73365 CAPLUS

DN 118:73365

OREF 118:12666h,12667a

TI Modulation of cardiac cyclic AMP metabolism by adenosine receptor agonists and antagonists

AU Ma, Hui; Green, Richard D.

CS Dep. Pharmacol., Univ. Illinois, Chicago, IL, 60612, USA

SO Molecular Pharmacology (1992), 42(5), 831-7
CODEN: MOPMA3; ISSN: 0026-895X

DT Journal

LA English

AB The mechanism(s) underlying adenosine receptor-mediated modulation of cardiac cAMP levels has been investigated using detergent-permeabilized embryonic chick ventricular myocytes. The β-adrenergic receptor agonist isoproterenol (ISO) stimulated adenylyl cyclase activity in detergent-permeabilized cells by 5-10-fold, with an EC50 value of 0.3 μM. Three adenosine receptor agonists, (R)-N6-phenylisopropyladenosine, N6-(3-iodo-4-aminobenzyl)adenosine, and 5'-N-ethylcarboxamidoadenosine, inhibited ISO (10 μM)-stimulated adenylyl cyclase activity in a concentration-dependent manner. The maximum inhibition of the ISO-stimulated adenylyl cyclase activity by (R)-N6-phenylisopropyladenosine (10 μM) was 30-40%. This inhibition was antagonized by the adenosine receptor antagonists xanthine amine congener and 8-cyclopentyl-1,3-dipropylxanthine and was abolished by pertussis toxin treatment, suggesting that the inhibition of adenylyl

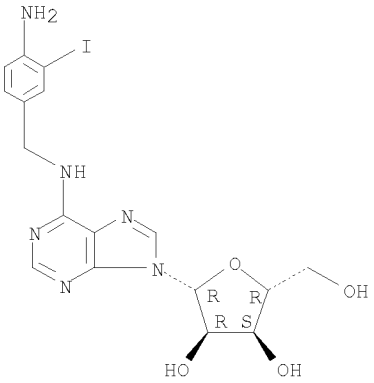
cyclase activity is mediated by A1 adenosine receptors acting via a pertussis toxin-sensitive guanine nucleotide-binding protein (G protein). Because the adenosine receptor agonists had no detectable effect on phosphodiesterase activity, the adenosine receptor-mediated inhibition of adenylyl cyclase activity appears to account for the cAMP-lowering effect of adenosine receptor agonists seen in intact cardiac myocytes. Moreover, two A1 adenosine receptor antagonists, 8-cyclopentyl-1,3-dipropylxanthine and 3-(4-amino)phenethyl-1-propyl-8-cyclopentylxanthine, stimulated basal adenylyl cyclase activity in the absence of an adenosine receptor agonist; this stimulation was abolished by pretreatment of the cells with pertussis toxin. We postulate that "precoupled" A1 adenosine receptor-G protein complexes, present in the cardiac myocytes, exert a tonic inhibitory influence on adenylyl cyclase activity and that some adenosine receptor antagonists remove this tonic inhibition by destabilizing these precoupled receptor-G protein complexes.

IT 98866-49-0
RL: BIOL (Biological study)
(cardiac cAMP metabolism modulation by, mechanism of)

RN 98866-49-0 CAPLUS

CN Adenosine, N-[(4-amino-3-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



OSC.G 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)

L4 ANSWER 35 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN

AN 1988:403328 CAPLUS

DN 109:3328

OREF 109:635a,638a

TI Photoaffinity labeling of adenosine receptors

AU Patel, Amrat; Linden, Joel

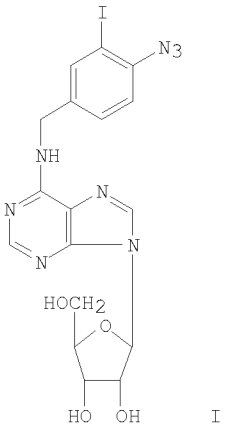
CS Sch. Med., Univ. Virginia, Charlottesville, VA, 22908, USA

SO Receptor Biochemistry and Methodology (1988), 11(Adenosine Recept.), 27-41
CODEN: RBMEEY; ISSN: 0888-7500

DT Journal

LA English

GI



I

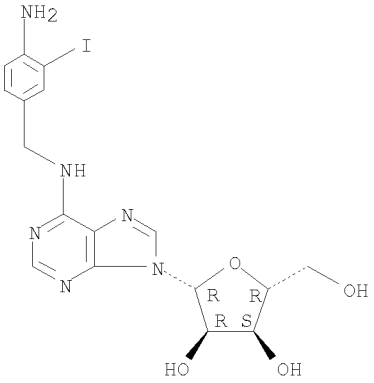
AB N6-3-125Iodo-4-azidobenzyladenosine (I) was prepared and its ability to photoaffinity label adenosine A1 receptors in brain membrane prepns. from various laboratory animals was examined I (<5 nM) bound specifically and reversibly in the dark to a single class of adenosine receptors with a dissociation constant of .apprx.1 nM in rat brain membranes. On photolysis (exposure to UV light) I covalently labeled adenosine A1 receptors of apparent mol. weight of 34 kilodaltons (kDa). Photoincorporation of I into the 34-kDa peptide displayed stereospecificity in that R-phenylisopropyladenosine was a more potent inhibitor of photoincorporation than the S-isomer. Inhibition of covalent labeling by adenosine analogs exhibited a potency order typical of A1-receptors. Guanylylimidodiphosphate inhibited covalent incorporation of I consistent with the agonist nature of this compound S6-Nitrobenzylthioinosine, which binds to the adenosine transport protein, failed to decrease I incorporation by the A1-receptor. Photoaffinity labeling of 6 different sources of A1-receptor did not reveal any species or tissue variations. Thus, differences in affinities of radioligands between species and tissues may not be related to the A1-adenosine receptor binding subunit.

IT 98866-49-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with sodium azide)

RN 98866-49-0 CAPLUS

CN Adenosine, N-[(4-amino-3-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

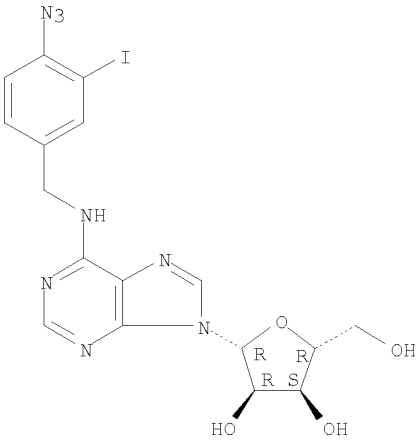


IT 98849-99-1 106719-48-6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of, as purinergic A1 receptor photoaffinity label)

RN 98849-99-1 CAPLUS

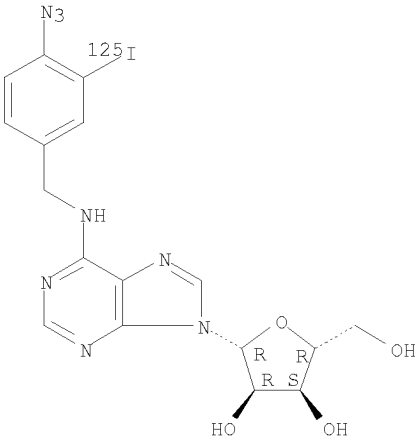
CN Adenosine, N-[(4-azido-3-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



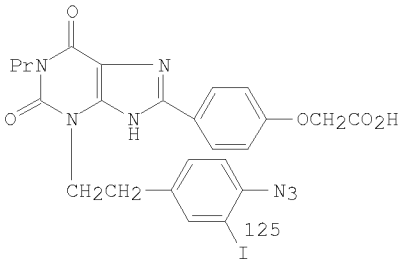
RN 106719-48-6 CAPLUS
CN Adenosine, N-[[4-azido-3-(iodo-125I)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



OSC.G 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 36 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 1988:150413 CAPLUS
DN 108:150413
OREF 108:24700h,24701a
TI Photoaffinity labeling adenosine A1 receptors with an antagonist iodine-125-labeled aryl azide derivative of 8-phenylxanthine
AU Earl, Craig Q.; Patel, Amrat; Craig, Rebecca H.; Daluge, Susan M.; Linden, Joel
CS Sch. Med., Univ. Virginia, Charlottesville, VA, 22908, USA
SO Journal of Medicinal Chemistry (1988), 31(4), 752-6
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
OS CASREACT 108:150413
GI



I

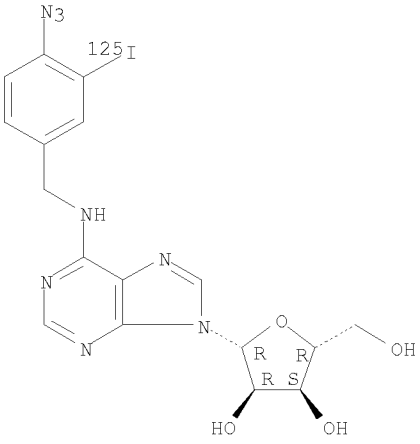
AB A series of 125I-labeled 8-phenylxanthines with photoactive aryl azide groups on the 1- or 3-position of the xanthine ring, e.g., I was prepared A 3-azidophenethyl derivative was found to be optimal for use as an antagonist photoaffinity label for adenosine A1 receptors. Following photoactivation, radioactivity was covalently and specifically incorporated into a 34,000-dalton and, to a lesser extent, into a 24,000-dalton polypeptide of rat brain membranes. Photoincorporation into both polypeptides was competitively inhibited by adenosine analogs with a potency order typical of adenosine A1 receptors, but the 24,000-dalton polypeptide bound both agonists and antagonists with lower affinity than the 34,000-dalton polypeptide. Specific photolabeling of receptors in brain membranes of rat, guinea pig, dog, and cow did not show any variation in the 34,000-dalton adenosine receptor binding subunit. The adenosine agonist photoaffinity label [125I]N6-(4-azido-3-iodobenzyl)adenosine also specifically photolabeled the 34,000-dalton polypeptide, but photoincorporation of the agonist was less efficient than the antagonist and, unlike the antagonist, was greatly reduced by guanosine 5'-(β,γ-imidotriphosphate). The results indicate that the antagonist photoaffinity label may be more useful than agonists particularly for labeling uncoupled receptors.

IT 106719-48-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and photoaffinity labeling by, of adenosine A1 receptors)

RN 106719-48-6 CAPLUS

CN Adenosine, N-[[4-azido-3-(iodo-125I)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

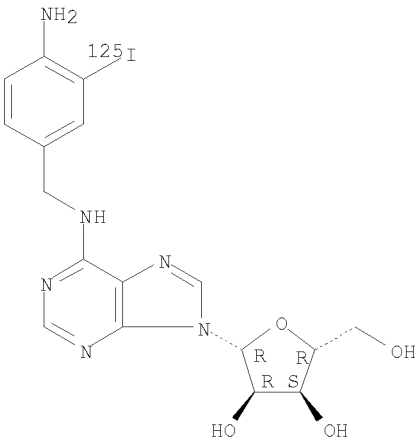


IT 95523-14-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, diazotization, and azide formation of)

RN 95523-14-1 CAPLUS

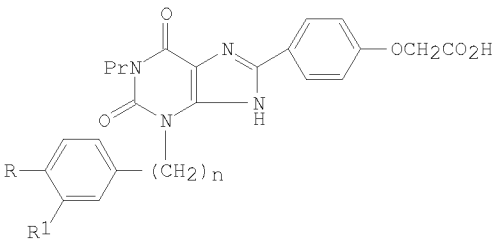
CN Adenosine, N-[[4-amino-3-(iodo-125I)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



OSC.G 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L4 ANSWER 37 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 1988:138785 CAPLUS
DN 108:138785
OREF 108:22655a,22658a
TI Iodine-125-labeled 8-phenylxanthine derivatives: antagonist radioligands for adenosine A1 receptors
AU Linden, Joel; Patel, Amrat; Earl, Craig Q.; Craig, Rebecca H.; Daluge, Susan M.
CS Sch. Med., Univ. Virginia, Charlottesville, VA, 22908, USA
SO Journal of Medicinal Chemistry (1988), 31(4), 745-51
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
OS CASREACT 108:138785
GI



I

AB 8-Phenylxanthine derivs. I (n = 1, 2; R = NH2, N3; R1 = H, iodo), were prepared with oxyacetic acid on the para phenyl position to increase aqueous solubility and minimize nonspecific binding and iodinatable groups on the 1- or 3-position of the xanthine ring. The structure-activity relationship for binding of these compds. to A1 adenosine receptors of bovine and rat brain and A2 receptors of human platelets was examined The addition of arylamine or photosensitive aryl azide groups to the 3-position of xanthine had little effect on A1 binding affinity with or without iodination, whereas substitutions at the 1-position caused greatly reduced A1 binding affinity. The addition of an aminobenzyl group to the 3-position of the xanthine had little effect on A2 binding affinity, but 3-aminophenethyl substitution decreased A2 binding affinity. Two acidic 3-(arylamino)-8-phenylxanthine derivs. were labeled with 125I and evaluated as A1 receptor radioligands. The new radioligands bound to A1 receptors with KD values of 1-1.25 nM. Specific binding represented >80% of total binding. High concns. of NaCl or other salts increased the binding affinity of acidic but not neutral antagonists, suggesting that interactions between ionized xanthines and receptors may be affected significantly by changes in ionic strength. On the basis of binding

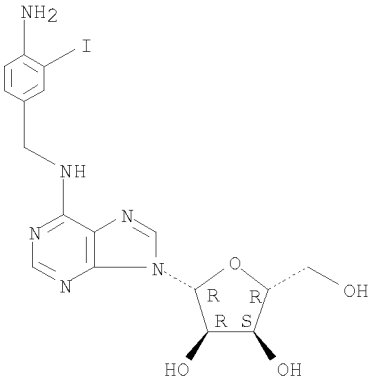
studies with these antagonists and isotope dilution with the agonist [125I]-N6-(4-amino-3-iodobenzyl)adenosine, multiple agonist affinity states of A1 receptors were identified.

IT 98866-49-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and binding of, to adenosine receptors)

RN 98866-49-0 CAPLUS

CN Adenosine, N-[(4-amino-3-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



OSC.G 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)

L4 ANSWER 38 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN

AN 1987:81170 CAPLUS

DN 106:81170

OREF 106:13261a,13264a

TI Synthesis and characterization of new adenosine A1 receptor radioligands, N6-3-125iodo-4-aminobenzyladenosine, and photoaffinity probe, N6-3-125iodo-4-azidobenzyladenosine

AU Patel, Amratlal P.

CS Health Sci. Cent., Univ. Oklahoma, Norman, OK, USA

SO (1986) 99 pp. Avail.: Univ. Microfilms Int., Order No. DA8616811
From: Diss. Abstr. Int. B 1986, 47(6), 2390

DT Dissertation

LA English

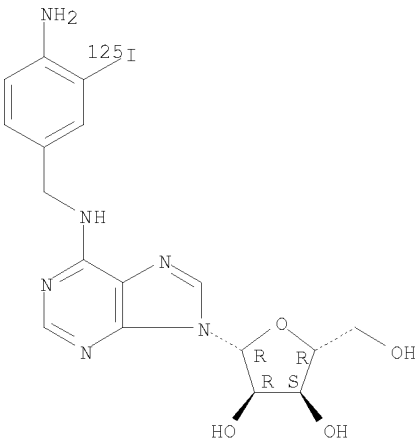
AB Unavailable

IT 95523-14-1P 106719-48-6P
RL: PREP (Preparation)
(preparation and adenosine A1 receptor binding by)

RN 95523-14-1 CAPLUS

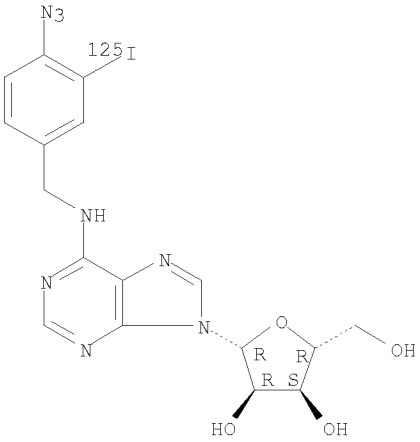
CN Adenosine, N-[[4-amino-3-(iodo-125I)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



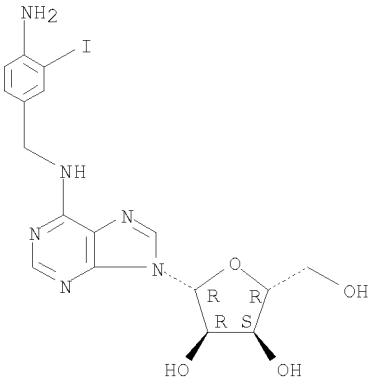
RN 106719-48-6 CAPLUS
CN Adenosine, N-[[4-azido-3-(iodo-125I)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



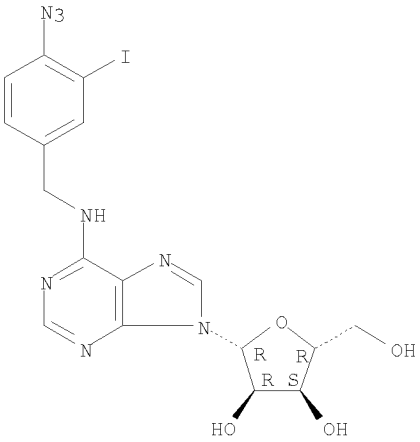
L4 ANSWER 39 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 1985:574900 CAPLUS
DN 103:174900
OREF 103:28062h,28063a
TI Specific photoaffinity labeling of inhibitory adenosine receptors
AU Choca, Jose Ignacio; Kwatra, Madan M.; Hosey, M. Marlene; Green, Richard D.
CS Coll. Med., Univ. Illinois, Chicago, IL, 60612, USA
SO Biochemical and Biophysical Research Communications (1985), 131(1), 115-21
CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English
AB N6(L-Phenylisopropyl)adenosine (L-PIA) and N6(3-iodo-4-azido benzl)-adenosine (IAzBA) inhibit the adenylate cyclase activity in synaptic membranes of chick cerebellum via Ri adenosine receptors. [3H]L-PIA and [125I]IAzBA bind to these membranes with Kd values of .apprx.1 nM and maximum binding values of .apprx.1000 fmol/mg protein. Photolysis of [125I]IAzBA bound to synaptic membranes results in the specific incorporation of radioactivity into a protein with a relative mol. weight of 36,000. This photoincorporation is blocked by simultaneous exposure to L-PIA, theophylline (an adenosine receptor antagonist), or guanylylimidodiphosphate, but not by cytosine, suggesting that the 36,000-dalton protein is the Ri adenosine receptor or a subunit of the receptor that contains the adenosine-binding site.
IT 98866-49-0
RL: ANST (Analytical study)
(iodoazidobenzyladenosine formation from)
RN 98866-49-0 CAPLUS
CN Adenosine, N-[(4-amino-3-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 98849-99-1P
RL: PREP (Preparation)
(preparation of, adenosine receptor of brain synapse determination by photoaffinity labeling in relation to)
RN 98849-99-1 CAPLUS
CN Adenosine, N-[(4-azido-3-iodophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 40 OF 40 CAPLUS COPYRIGHT 2010 ACS on STN
AN 1985:143648 CAPLUS
DN 102:143648
OREF 102:22439a,22442a
TI [125I]Aminobenzyladenosine, a new radioligand with improved specific binding to adenosine receptors in heart
AU Linden, Joel; Patel, Amrat; Sadek, Samy
CS Oklahoma Med. Res. Found., Oklahoma City, OK, USA
SO Circulation Research (1985), 56(2), 279-84
CODEN: CIRUAL; ISSN: 0009-7330
DT Journal
LA English
AB The d. of adenosine [58-61-7] receptors in membranes derived from rat hearts is 25 times lower than the d. of receptors in rat brain membranes. Consequently, adenosine radioligands which are useful in brain, such as l-[3H]phenylisopropyladenosine, [3H]cyclohexyladenosine, [3H]-2-chloroadenosine, and l-[125I]hydroxyphenylisopropyladenosine [95523-12-9], are of limited usefulness in heart, due to a high ratio of nonspecific to specific binding. Thus, the radioligand, [125I]-N6-4-aminobenzyladenosine [95523-14-1] was prepared and this binds to rat heart membranes with 1/6 the nonspecific binding of the other radioligands. [125I]-N6-4-aminobenzyladenosine bound to rat ventricle membranes with (an affinity) KD equivalent to that of

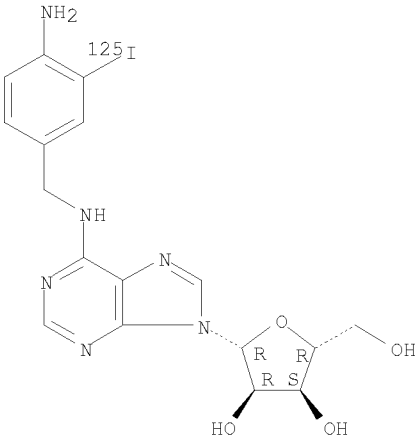
l-[125I]hydroxyphenylisopropyladenosine and a(maximum binding capacity) Bmax of 15.2 fmol/mg protein. [125I]-N6-4-aminobenzyladenosine bound with a higher affinity to brain (KD = 1.93 nM) than to heart membranes (KD = 11.6 nM). At the radioligand KD, 60% of the total [125I]-N6-4-aminobenzyladenosine bound to heart membranes was specifically bound. Iodination of aminobenzyladenosine increased its affinity for the adenosine receptor by 22-fold, possibly due to a steric or hydrophobic effect of I. The new ligand was a full adenosine agonist based on its ability to inhibit cyclic AMP [60-92-4] accumulation in isolated embryonic chick heart cells and rat adipocytes. [125I]-N6-4-Aminobenzyladenosine bound to a single affinity site and was displaced from cardiac and brain adenosine receptors by other adenosine analogs with a potency order of l-phenylisopropyladenosine > 5'-N-ethylcarboxamide adenosine. Apparently, the radiolignad binds to an Ri adenosine receptor.

IT 95523-14-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as adenosine receptor ligand of heart)

RN 95523-14-1 CAPLUS

CN Adenosine, N-[[4-amino-3-(iodo-125I)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



OSC.G 31 THERE ARE 31 CAPLUS RECORDS THAT CITE THIS RECORD (32 CITINGS)